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BULLETIN

OF THE NEW YORK ACADEMY OF MEDICINE

Original Articles by

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MANAGEMENT OF PERIPHERAL VASCULAR DISEASE

Transcription of a Panel Meeting on Therapeutics

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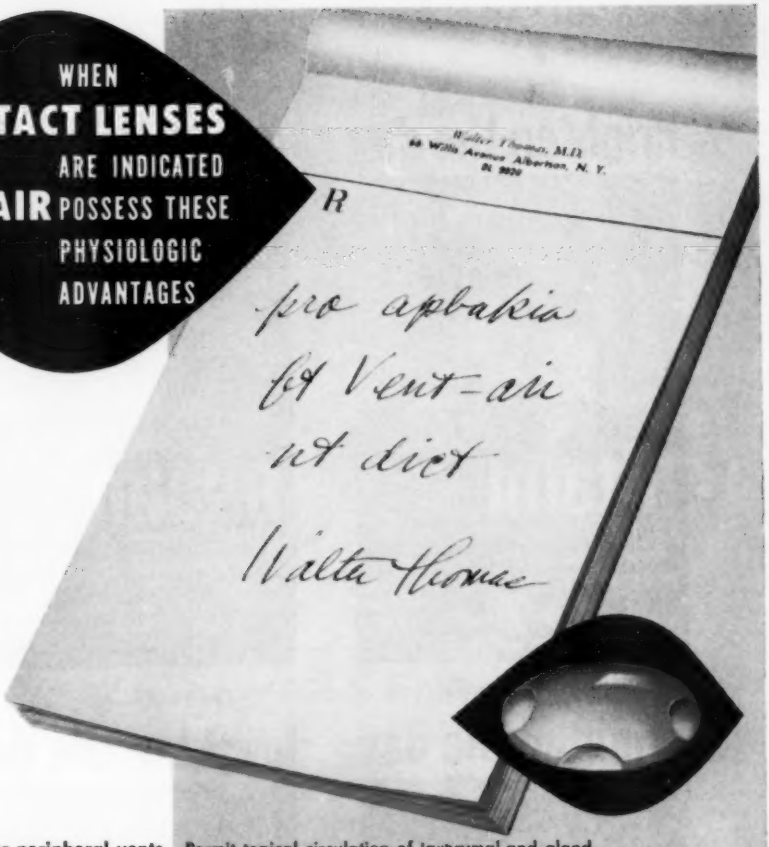

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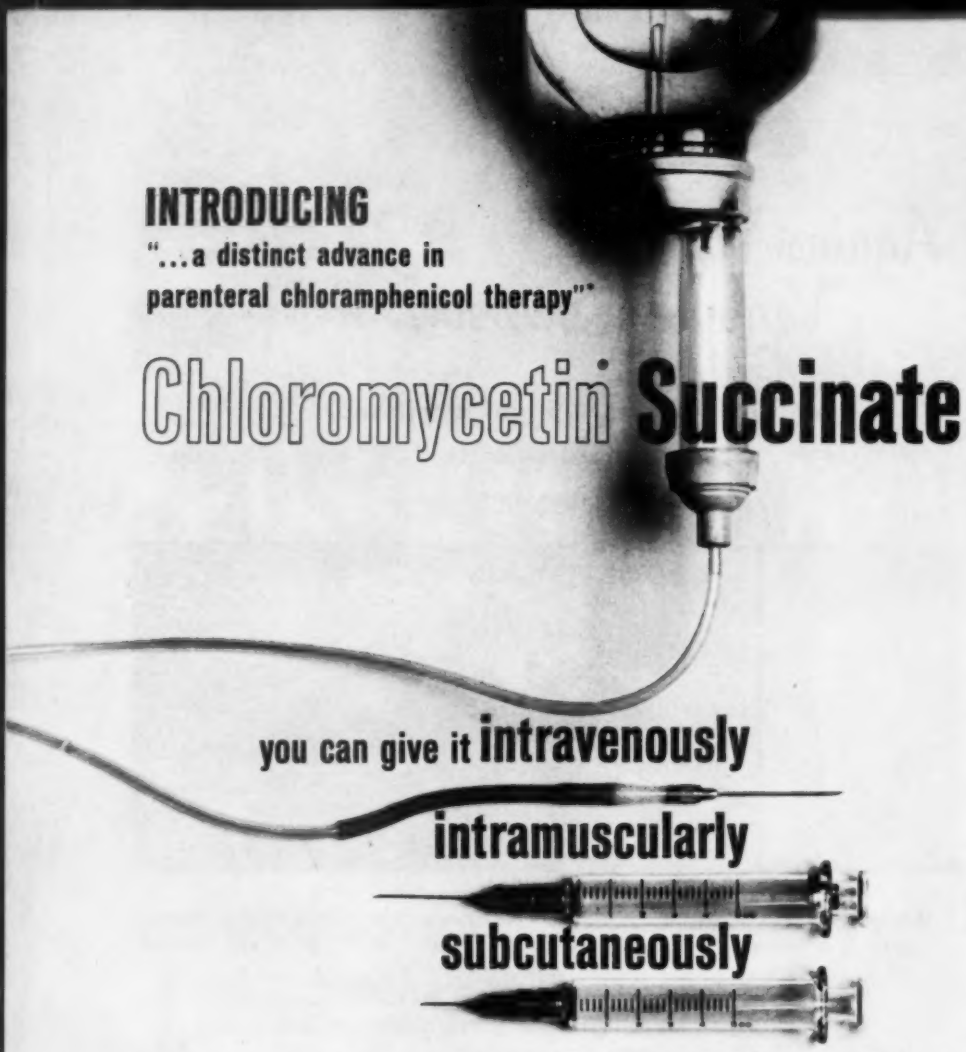

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*Ross, S.; Puig, J. R., & Zaremba, E. A., in Welch, H., & Martí-Ibañez, F.: Antibiotics Annual 1957-1958, New York, Medical Encyclopedia, Inc., 1958, p. 817.

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1. A. M. A. Arch. Int. Med., *99*:346, 1957.
2. Am. J. Obst. & Gynec., *70*:1309, 1955.
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ROBERT L. CRAIG, *Editor*

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BULLETIN OF
THE NEW YORK ACADEMY
OF MEDICINE

VOL. 35, NO. 4 APRIL 1959

THE ACADEMY IN TRANSITION

*Address of the President**

ROBERT L. LEVY

TO-NIGHT, mine is a dual role—that of new incumbent and of his predecessor. This combination favors the audience; for, one speech, traditionally a required item on the program, can be eliminated without breach of custom. I am deeply sensible of the distinction implied in having been asked to continue in office for a second term. Although not unaware of the responsibilities involved, it gives me pleasure to accept this opportunity for further service.

To review, in detail, all that has transpired here during 1958, is not feasible. A full account will be given in the Annual Report of the Academy. Mention should be made, however, of the many spirited and instructive meetings of the Trustees and Council, as well as of the Standing Committees which activate the Academy's varied functions. These sessions furnish a potent stimulus to progressive thought and action. Throughout the year, I have enjoyed a close association with the Director, Dr. Howard Reid Craig, who has been counselor and guide. His experience and sound judgment are paramount in all the

* Delivered at the Annual Meeting of The New York Academy of Medicine, January 8, 1959.

affairs of the Academy.

In accordance with previous practice, various responsible members of the full-time staff were requested to submit summaries of the year's doings in their respective departments. In condensed form, these now follow.

Summarized Reports

The Director—Dr. Howard Reid Craig. In the year 1958, there has been an increase in the budgeted expenses of the Academy, due largely to advances in salaries, and the greater cost of labor and materials. Despite a policy of economy, the Survey Committee urgently recommended that the cafeteria be remodeled and modernized, in order to provide proper eating facilities for the staff, the employees and visitors. After prompt approval by the Council, this project was completed, at a cost of thirteen thousand dollars and with gratifying results. The same Committee has made other recommendations, also duly approved, which involve additional expenses. This means that, in 1959 and 1960, there must be found new sources of revenue for general purposes.

Two recent accomplishments stand out in importance and in their implications for the future. The first concerns the Survey Committee. Under the chairmanship of Dr. William Barclay Parsons, it has completed its work after eight months of intensive activity. The firm of Cresap, McCormick and Paget, Management Consultants, was engaged to study the operations of the Academy and make recommendations with respect to overall administration, the Library and financial management. Its report, together with those of the eight Subcommittees of the Survey Committee, has been submitted to the Council and has been under consideration for the past three months. Some of the recommendations already have been put into effect, others are still under scrutiny, and a number can be effectuated only over a period of time. The final report, as approved by the Council, will appear in an early issue of the *Bulletin*.

The second significant achievement has been the initiation of a movement to establish a Central Depository Library, designed to serve all of the major medical libraries in the New York metropolitan area. Under this plan, each institution would maintain its own current working library, using the depository for its surplus. Because the Academy Library is the largest and most thoroughly manned in this part of the

country, it would seem sound policy to locate such a depository in close juxtaposition to the Academy. A suitable building, satisfactory with respect to location, size and construction, is available. Last March, approximately one hundred librarians, representing all the medical libraries in the metropolitan area, held a formal meeting at the Academy and, having endorsed the project, appointed a committee to work out details of procedure. In June, a meeting was held with the Deans of the six New York medical colleges or their associates; also represented were two important research institutes. Although no definite commitments were possible, the urgency of the problem was recognized and enthusiastic approval was expressed.

It will require approximately one-and-a-half million dollars to acquire the necessary property, set up and organize such a library, and provide a pool from which material might be made available to other centers across the country. The cost is relatively small as compared with that of erecting new libraries within the various universities and institutes. This is a community effort and, as such, deserves financial help from Foundations and individuals who have at heart the encouragement of education and research. Support for this project is needed, and needed now.

The Library—Miss Gertrude L. Annan, Librarian. The Library's most important step in 1958 was participation in a plan for regional cooperation, as outlined in the report of the Director. The establishment of a depository library must await the raising of funds. Meantime, action is being taken to survey the holdings of current journals regularly received in eleven libraries. From this study, it is hoped that, without disproportionate cost to any one library, a wider coverage can be achieved. Equally important is a project, already initiated, to determine how much duplication may be eliminated among the less important, though necessary, journals which are always received gratis but demand processing and storing.

The Library has been impelled to curtail its purchases of peripheral material, not primarily medical. In order that such literature may be available when required, inter-library loans from non-medical libraries in the vicinity are possible. Such arrangements have been made with the Columbia University Library and the New York School of Social Work. Similar agreements will be sought with other local libraries.

It is of interest to note that, in the surveys of our readers made in November, 1957, and March, 1958, the percentage of the non-medical public coming to the Library was approximately 50 per cent. The percentage of Fellows of the Academy and their representatives coming to the Library in person was about 20 per cent; this is a considerable increase over comparable figures in 1947. The trend toward a rise in the number of readers has continued, in some degree, in 1958.

The generosity of the Friends of the Rare Book Room has made possible the acquisition of a number of cherished volumes. Additions to the collection of local manuscripts are always especially welcome.

The Committee on Public Health—Dr. Harry D. Kruse, Executive Secretary. In its report of a study of tranquilizing drugs, made two years ago, the Committee stated that some advertising literature not only contained exaggerated claims for the products described, but omitted, or gave small space to, contraindications and side effects. It was recommended that the Department of Health, with these points in mind, survey the literature issued by pharmaceutical manufacturers. The study just completed by the Health Department revealed a number of misleading methods of presenting ethical products. Since this unfair practice is nationwide, it would be most effectively controlled by Federal law. Consideration is being given to such action.

The Committee has concerned itself with two hazards to public health which are of increasing significance, namely, radiation and air pollution.

Uneasiness is said to have arisen over the presence of ionizing radiation in and around research installations, in waste materials from industries, and in medical and dental practice. This source of radiation is not to be confused with radioactive fall-out. In spite of authoritative statements that the dangers in radiation can be minimized by protection appropriate to the exposure, it has been reported that some persons have become so concerned about the risk as to refuse even diagnostic and therapeutic use of radiation. To ensure proper protection for both the general public and workers in occupations dealing with radiation, the Board of Health drafted an article containing appropriate provisions for the Sanitary Code of New York City. Invited to review the new section in draft form, the Committee offered several suggestions based on study by a subcommittee composed of authorities representing

radiology, dentistry and physics. Of special importance was a recommendation that no limitation should be imposed on the kind and amount of radiation that a physician or dentist may intentionally apply to a patient, in diagnosis or treatment. It was pointed out that persons under treatment or animals subjected to experimentation with isotopes may be a source of ionizing radiation, and it was suggested that methods be formulated for the handling of such patients and animals. These suggestions, among others, were incorporated in the Code as enacted in 1958.

In response to a request from former Governor Harriman, the Committee devoted considerable attention to atmospheric pollution other than contamination by radiation. Current thinking indicates that the effects of air pollution on health may be either acute or chronic. Several well-studied incidents have led to the belief that acute episodes may occur under unusual conditions of meteorology and terrain. Chronic effects are more elusive, but may have far greater significance. Long-term exposure to polluted air is under suspicion as a possible contributory cause of cancer of the lung and as an aggravating influence on existing cardiac and pulmonary disorders. In its report, the Committee urged more research to provide much-needed information in this field.

The Committee on Medical Education—Dr. Robert L. Craig, Executive Secretary. The following scientific programs were arranged: the Stated Meetings of the Academy; monthly panel meetings; a three-session course for general practitioners, dealing with "Practical Applications of Electrolyte and Fluid Balance"; the Postgraduate Week, which was concerned with "Research Contributions to Clinical Practice". The sessions of the Postgraduate Week were unusually well attended, due largely to the excellence of their content and the eminence of the speakers. The scientific exhibit was outstanding.

The Oppenheimer Lecture was given by Dr. Gunnar Biörck of Malmö, Sweden. The Ewing Lecture was delivered by Dr. Charles Berman, of the Transvaal, South Africa. The Sections on Microbiology and Pediatrics held a joint two-day symposium on "Viral Infections in Infancy and Childhood"; three of the nineteen lecturers were from foreign countries.

Under the Bowen-Brooks Scholarship Fund, a resident surgeon at

Memorial Hospital is now taking further training in chest surgery at the Brompton Hospital, London, England.

The Committee on Medical Information—Dr. Iago Galdston, Executive Secretary. As usual, many inquiries have been answered and a number of manuscripts, submitted by various weekly and monthly publications, have been reviewed.

The "Whither Medicine Pilot Study" has gone on. At a series of meetings, guest speakers have discussed the medical aspects of education, economics, industry, hospital services and the role of pharmaceutical houses. Eventually, this material will be assembled in book form.

The Committee has published three volumes: *Panic and Morale*, *The Impact of Antibiotics on Medicine*, and *The Family in Contemporary Society*.

The weekly FM program, "For Doctors Only", has been continued.

The annual Eastern States Health Education Conference was held at the Academy and was devoted to the topic "Toward a Philosophy of Public Health". The third conference of the Institute of Social and Historical Medicine was held at Arden House; its subject was "Nutrition".

In May, the Rockefeller Institute and the Academy acted as joint hosts for the annual meeting of the American Association for the History of Medicine.

The current series of "Lectures to the Laity" is entitled "Science—Man's Master or Servant?"

The Bulletin—Dr. Robert L. Craig, Secretary and Editor. The *Bulletin* has continued to publish original articles presented at various Academy meetings and functions. In addition, there have appeared abstracts of papers given at the meetings of the New York Pathological Society and at scientific sessions of the New York Heart Association.

The *Bulletin* is distributed gratis to all Fellows of the Academy. It has a wide circulation, both paid and exchange, in this country and abroad.

A Note on the Changing Scene

The rapid progress of science during the past several decades has exerted a powerful influence on medicine. Attitudes toward education,

research and practice have been subjected to basic modifications which will, and must, undergo further evolution. Tonight is not the time to dilate on this theme; but the Academy, through its Council, has realized the need for self-examination. The survey, to which reference already has been made, is finished, except for a special report on the Library. In brief, these are a few of the recommendations which have been approved:

1. There are to be three new appointees—a business manager, a director of public relations and fund-raising, and a coordinator of medical education. A Committee of Fellows will serve with each.

2. There will be created a Division of Publications and Medical Information, with the Editor of the *Bulletin* in charge.

3. There will be appointed a Committee on Special Studies, to replace the present Committee on Medical Information.

4. The Editorial Board of the *Bulletin* will be reorganized in a manner which should enable it to function more actively.

5. Three laymen, expert in the field of finance, will be asked to serve as consultants to the Investment Committee of the Trustees.

6. An Executive Committee, composed of the Officers of the Academy, with the Director as an *ex officio* member, is empowered to act for the Trustees and Council in emergencies.

Undoubtedly, there will be differences of opinion as to the wisdom of instituting some of the proposed innovations. Those who assumed responsibility for action may find a measure of comfort in a thought expressed by Alexander Pope in his "Essay on Criticism", written just two hundred and fifty years ago:

> "*'Tis with our judgments as our watches, none*
> *Go just alike, yet each believes his own.*"

CITATION AND PRESENTATION

OF THE

ACADEMY MEDAL*

TO

F. PEYTON ROUS, M.D.

C. P. Rhoads

Director, the Sloan-Kettering Institute for Cancer Research, New York, N. Y.

As years pass it becomes more frequently in order for the somewhat younger individual to speak publicly, in tribute to a somewhat older one. To perform this function a pupil of the senior is usually selected, or at least one who has some direct scientific or other reason to be indebted to the recipient of the honor. To discharge his duties properly, moreover, the payer of tribute is expected to bring forward some unique twist of phrase which will distinguish or make memorable his comment.

Until recently I have never had the honor of working with Peyton Rous, and I have no gift of words adequate to discharge properly my responsibility on this occasion. My contact with this man has been, however, of such a peculiar, and to me inspiring, nature as to lead me to acquiesce with the suggestion that I refer to it publicly, in tribute to this notable recipient of the Academy Medal.

Since it is usual and useful to refer to biographical matters, I would remind you that Dr. Rous was graduated from Johns Hopkins University in 1900, and received his medical degree in 1905. He interned at the Hopkins Hospital in medicine, became interested in pathology and continued this interest at Michigan. He was called to the Rockefeller Institute in 1909 and has been there, and a leader there, since that time.

Recall, if you will, the role of Hopkins in the revolution in medical teaching and research under way then, the inspiration given to younger men by its very great faculty, and its unique point of view.

The problem of the control of cancer disease mounts steadily

* Presented at the Annual Meeting of The New York Academy of Medicine, January 8, 1959.

F. PEYTON ROUS, M.D.

in importance. The major steps toward its solution have been made by a relatively small number of individuals. Among these Peyton Rous was, in 1911, one of the first. Our modern knowledge of the neoplastic process has been constructed to a large extent around his contributions.

His original demonstration of the cell-free transmission of fowl neoplasms was complete, and at the same time revolutionary. It remained a storm center of discussion among workers in cancer research for forty years. Its significance for an understanding of cancer has been fully appreciated only recently. This work remains a landmark not only in the field of its direct application, but also in virology as a whole.

But Peyton Rous saw beyond the circumscribed area of a single technique. When its possibilities were temporarily exhausted by the limited knowledge of the time, he turned, with similar skill, to other fields.

Modern hematology, replete with knowledge and procedures, gives little hint of how mysterious were the mechanisms of blood generation and destruction thirty years ago. Transfusion was a major surgical undertaking. The preservation of blood was inconceivable, its destruction little understood, and its production a mystery. "Anemia" was a diagnosis almost as useless as "fever" had been before our knowledge of the bacterial etiology of disease. Peyton Rous and his associates went far to illuminate these biological recesses.

Immunology was also the gainer by his work. New knowledge of the source of antibodies was made available. The discovery of hydrocarbon carcinogens and of a virus-induced cancer of the mammal by Shope brought additional new tools to hand. The complementary actions of the carcinogens and tumor viruses became a major step forward in cancer research. It contributed much to our thinking on hidden or latent viruses that may spring into action under some apparently unrelated stimulus.

I have recounted, perhaps inadequately, some part of the formal record. May I now refer to a more personal and largely unrecorded aspect of his work. This was his contact with and influence on younger men.

As a young pathologist just entering the field of investigative medicine, I had early contact with Dr. Rous in his capacity as editor of the *Journal of Experimental Medicine*. I am afraid that I was a brash young man at the time, distinctly overestimating the importance of the manu-

script I had submitted. In retrospect, this was not surprising since the work had no value whatever.

Dr. Rous, gravely and patiently, reviewed my efforts with me, demolished my conclusions, refuted my claims and made clear the proper use of my native tongue. He then rebuilt on the ruins such a clear picture of the problem, and the procedure required to solve it, that my conceit was converted almost imperceptibly to inspiration, my enthusiasm to resolution. As I left the generous, patient, and kindly man, I was no longer the same individual. I was, however, wholly convinced that if I worked very assiduously, with the greatest vigor, for a very long time, perhaps I could make a real contribution.

Nothing, please be assured, could have turned me then from a life in medical science.

And realize, if you will, that the world of medical research is now strongly influenced by many, many individuals, much more deserving than I, who chose that career because of Dr. Rous' unique capacity for making inspiration stick and become an irrevocable resolution.

May I then, express my deep feeling and that of many others by the following words in appreciation of Dr. Peyton Rous:

DETERMINATION WITHOUT DOGMATISM
CONSISTENCY WITH CONSIDERATION
WISDOM WITH GENEROSITY
A MOST BELOVED PHYSICIAN
TO WHOM SCIENCE OWES SO MUCH
TO WHOM THE CHARACTER OF SCIENTISTS OWES MORE

And may I then, Peyton, present to you the Medal of The New York Academy of Medicine, a small recognition of what you have meant to so many.

CITATION AND PRESENTATION OF THE ACADEMY PLAQUE* TO MONTGOMERY B. ANGELL, ESQ.

HOWARD REID CRAIG
Director, The New York Academy of Medicine

IT HAS BEEN my privilege and pleasure, over the past few years, to have been asked by the Academy Committee on Honors to present, on behalf of the Academy, this Plaque. It reads, "For outstanding service to The New York Academy of Medicine." However, to me the implications are far broader and deeper than the word "service" connotes. Fortunately, the bestowal of the Plaque is not limited to physicians or to Fellows of the Academy, and for that reason takes on added significance. It recognizes, beyond the limits of tangible services, extraordinary interest in the affairs of the Academy and real friendships that have been engendered by mutual association. Our guest this evening fulfills these criteria to an outstanding degree.

Educated at Princeton and at the Harvard Law School where he was a member of the Law Review, our friend joined the Interstate Commerce Commission until the outbreak of World War I. He entered the Armed Services as a captain of infantry, was later promoted to major and served with the 81st Infantry Division in the Vosges and the Meuse-Argonne offensives, in recognition of which he received the Croix de Guerre with gold star and a French Army Corps Citation.

Returning from the war, he went to the Treasury Department in Washington and later to the General Counsel's office of the Federal Reserve Board. In 1921, he became associated with the firm of Stetson, Jennings & Russell, which later became Davis Polk Wardwell Sunderland & Kiendl, which firm has been counsel to the Academy for over thirty-five years and of which our guest is now a senior partner.

He is a lawyer scholar, having contributed articles dealing with

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taxation to many law reviews and to the Practicing Law Institute. So much for very bare biographical facts.

It was our guest who, in the nineteen-thirties, during the Directorship of Dr. John A. Hartwell, with great labor and skill, engineered, before the Department of Internal Revenue, the establishment of The New York Academy of Medicine as a tax-exempt, educational institution. This is easy to recount in retrospect, but it involved a knowledge and an insight into the affairs and the philosophy of the Academy that far transcended any routine tax procedure. For this the Academy will always be grateful.

And then again in 1949, it seemed expedient, for other reasons, to have the Academy's tax position reviewed and reaffirmed. Once more our friend took the bit in his teeth, accumulated a tremendous mass of data and exhibits of varied kinds, prepared his briefs or arguments or whatever attorneys call them, and again the position of the Academy was affirmed. My telling is terse, but I assure you that the work involved was enormous.

Finally, during the course of the recent Academy survey which President Levy has noted, our guest served most helpfully and effectively on the Committee on Finance. Meeting as a member of this Committee, his counsel, his breadth of view and his inside knowledge of the Academy aided immeasurably in bringing out of that Committee constructive and practical recommendations in respect to the management of the Academy's external finances.

But, more than all this, the Administration of the Academy has always felt that in our guest we had not only wise counsel, but a real friend. Too often, business or legal relationships are casual, cursory and cold. The Academy has been fortunate, indeed, to have enjoyed a relationship with our guest and his confreres that has been one, not only of confidence and trust, but, as well, of warmth and friendship.

I have great personal pleasure and satisfaction in presenting this Plaque which is inscribed:

PRESENTED TO
MONTGOMERY B. ANGELL
IN RECOGNITION OF
OUTSTANDING SERVICE TO
THE NEW YORK
ACADEMY OF MEDICINE

MANAGEMENT OF PORTAL HYPERTENSION*

ARTHUR B. VOORHEES, JR.

Instructor, Department of Surgery, College of Physicians and Surgeons, Columbia University; Assistant Attending Surgeon, The Presbyterian Hospital, New York, N. Y.

I CONSIDER it a privilege to speak to you on the subject of portal hypertension and, more specifically, on the clinical management of cases that exhibit the syndrome. It is a subject of particular interest to me, and I feel most fortunate that my association with Dr. A. H. Blakemore has enabled me to become an observer, a recorder, and in a small way, a contributor to the enormous amount of pioneer work that he has done in this field.

A transient elevated pressure within the portal system exists in many normal physiological states; for example, in direct response to histamine or epinephrine, in response to the Valsalva maneuver or following hepatic plexus stimulation. A reversible elevated pressure also exists in many pathological states, such as congestive heart failure, bronchial asthma and pericardial effusions. However, the irreversible pathological states of constrictive pericarditis, inferior vena cava, hepatic vein, intrahepatic and extra-hepatic venous obstruction are of particular interest to the physician because of the usually striking anatomical deformities which lead to the diagnosis of portal hypertension. The surgeon shares an equal interest because of his increasing capacity to correct some of its causes or results.

This evening I wish to limit my discussion to the most frequently encountered form of portal hypertension, that which is secondary to an intrahepatic venous block caused by portal cirrhosis. It is generally believed that hypertension is due to a deformed intrahepatic vascular anatomy, which is caused by hepatic cell death followed by irregular and eccentric nodular regeneration. The expanding nodules obliterate or compress some of the sinusoids and portal vein radicals, while other sinusoids dilate and bring about ease of communication between hepatic

* Presented at the Postgraduate Week, *Research Contributions to Clinical Practice*, of The New York Academy of Medicine, October 16, 1958.

TABLE I—PORTACAVAL SHUNT FOR PORTAL HYPERTENSION
1943-1958

Intrahepatic Block	318
Attempted	8
Extrahepatic Block	70
Attempted	6

arterioles and portal vein branches. Through death of the lobule and eccentric regeneration, the central vein comes to be situated near the periphery of the nodule; therefore, portal venous and hepatic arterial blood can pass directly to the central vein and thus by-pass much of the parenchyma. These vascular changes, summarized by Popper & Shaffner[1], are of particular importance because they set the stage for portal hypertension and for diversion of the blood supply from the regenerating hepatic cell. Hemorrhage from varices is likely, and each hepatic cell is on the brink of anoxia.

General as these terms have been, they govern much in our philosophy of management and explain why we are reluctant to subject a patient to the stress of an operation following a shock-producing hemorrhage; why we are anxious to stop hemorrhage and not just keep up with it by transfusion; and why we are not surprised to see evidence of diminished liver function following relatively minor bleeding from varices.

The bulk of experience which I wish to summarize has been derived from a series of 318 cases collected from 1943 to 1958 (Table I). From this point on I should like to take up four major management problems in the same sequential order in which they frequently confront the physician.

Hemorrhage from Esophageal Varices: Bleeding from varices is not always large in amount, but frequently it is, and at such times it requires the facilities of a hospital for control. The diagnosis of bleeding from varices is not always easy to make, since the bleeding must be differentiated from that of peptic ulcer. In our overall series there has been a coincident ulcer or ulcer history in 25 per cent of the cases, and for this reason an esophagram on an emergency basis is undertaken if the

TABLE II—HEMORRHAGE CONTROL—60 CONSECUTIVE CASES
1956-1958

Current Bleeding			25
	No Ascites	Balloon Stopped	6
		Balloon Failed to Stop	3
		Stopped Spontaneously	3
	Ascites	Balloon Stopped	3
		Balloon Failed to Stop	10

patient's condition permits. The esophageal balloon can be used as a differential diagnostic tool to aid in distinguishing esophageal from gastric bleeding. Often this is a clear-cut separation, but it is by no means absolute. General support in the form of oxygen, blood, and bed rest is given and, if there is evidence of continued bleeding, balloon tamponage is favored as a method of control.

Linton[2] passes a large balloon into the stomach, inflates it by a double-lumen tube and applies two pounds of traction for 8 to 12 hours, during which time the blood volume is restored and the patient is prepared for transthoracic esophagotomy and ligature of varices. All patients are committed to operation. Linton reports an 80 per cent success rate, but he does not delineate the severity of the disease in which this result was achieved.

Blakemore advocates passage of a double balloon, triple-lumened tube for compression tamponage. He thereby avoids committing all patients to immediate operation and reserves operative ligation for those who fail to be controlled by compression alone.

The esophageal balloon tube is a useful, life-saving but treacherous device. We are fully aware of its capacity to lead to aspiration, asphyxiation, and esophageal erosions. Most of these tragedies can be averted only through strict attention by the physician and watchfulness on the part of specifically trained personnel. A recent series reported by Conn[3] serves to emphasize that, if inadequately supervised, compression tamponage by the esophageal balloon can lead to serious complications, many resulting in death.

A series of 60 consecutive cases was selected because of uniformity

TABLE III—DEFINITIVE THERAPY—60 CONSECUTIVE CASES
1956-1958

				Deaths
Current Bleeding	25			
No Ascites	12	PC Shunt	12	1
Ascites	13	PC Shunt	3	0
		Varices Suture	2	0
		No Operation	8	8
Previous Bleeding	35			
No Ascites	26	PC Shunt	26	1
Ascites	9	PC Shunt	9	2

of management (Table II). Balloon tamponage failed to stop bleeding in roughly one-half the cases that were actively bleeding on admission to the hospital. Our experience has undoubtedly been shared by other surgeons and has led to other therapeutic attempts, all operative. Specifically, I am referring to segmental gastric and esophageal resections and the emergency portacaval shunt. Although a substantial percentage of patients survive these operations, it is highly unlikely that this percentage will approach that of patients who survive a portacaval shunt electively performed after hemorrhage has been conservatively controlled. If these procedures are reserved for the individuals in whom hemorrhage cannot be controlled, the risks would be prohibitive. For these reasons, we currently advocate early esophageal balloon tamponage without traction; and if this fails to stop bleeding, we recommend simple gastrotomy with direct suture of gastric varices, the usual source of bleeding in instances where esophageal balloon tamponage has failed (Table III).

During episodes of massive bleeding from varices, coma is a common complication. Although we are reluctant to accept the ammonia intoxication syndrome as the sole etiological mechanism, the concept has provided certain valuable therapeutic tools. Mechanically ridding the gastrointestinal tract of substrate for bacterial action and modifying bacterial activity by antibiotics can produce a dramatic awakening in many instances. The use of glutamic acid or arginine has, in our ex-

perience, been of little proven value. Our impressions have been comparable to those recently reported by Reynolds, Redeker, and Davis[4].

Preoperative Management and Case Selection: Assuming that hemorrhage has been brought under control, the next step is to prepare the patient for some therapeutic measure that will prevent repetition of hemorrhage. Although the precise mechanism of initiation of bleeding from varices is not always known, it has been observed that once an individual case has bled, repetition is likely. Preparation of the patient is synonymous with a strict medical program for the treatment of cirrhosis; and to date, that which has been set forth by Patek has been the most acceptable. In 1953, Blakemore and Fitzpatrick[5] set forth what they felt were critical levels of liver function studies dividing the good from the bad surgical risks. The good risk patient had a cephalin flocculation of 2 + or less, a BSP retention of 30 per cent or less in one half hour, a serum albumin of 3.5 gm. per cent or more and a serum bilirubin of 1.5 mgm. per cent or less. During the past three years an addition has been made to these criteria which seems to be of paramount importance. If, while on a well-controlled medical regimen in a hospital, the patient can demonstrate the capacity to improve a depressed level of liver function or to sustain a high level, then the postoperative mortality will be less than 5 per cent.

It is, therefore, our practice to advise definitive surgical therapy for only those cases in which a reserve capacity of the liver can be demonstrated and to discourage surgical therapy for those cases in which liver function continues to deteriorate despite a good medical regimen.

Selection of Operation: At present there are three general classes of operations for the control of bleeding from gastric and esophageal varices:

1. Interruption of the blood supply to the varices.
2. Excision of part or all of the varices-bearing segment of the upper gastrointestinal tract.
3. Decompression of the portal venous bed by a portacaval shunt.

In regard to interruption of the blood supply to the varices, be it accomplished by direct suture as advocated by Crile[6] or blood vessel interruption as advocated by Tanner[7], control of bleeding is at best temporary. Excision of part or all of the varices-bearing segment of the upper gastrointestinal tract can be an effective method of controlling hemorrhage. The main disadvantage is that it is frequently attended by

TABLE IV—EXPECTED SURVIVAL FOLLOWING PORTACAVAL SHUNT
(Operative deaths excluded)

Year	*Approx. % Alive*
1st	90%
2nd	
3rd	
4th	60%
5th	
6th	
7th	30%
8th	20%

nutritional disturbances, undesirable in the long term therapy of cirrhosis. For this reason, we have reserved these procedures for those cases in which a portacaval shunt cannot be performed.

The portacaval shunt, in our opinion, remains the procedure of choice and, of the possible varieties, the end-to-side portal vein-to-vena cava anastomosis is the most uniformly efficient. The instance of subsequent hemorrhage in a series of 318 has been 15 per cent for the portal vein-to-vena cava shunt and 45 per cent for the splenorenal shunt. A significant number of the failures of portal vein-to-vena cava shunt can be attributed to mechanically poor anastomoses resulting from an unusually small or partially thrombosed portal vein. In selected instances, the use of splenoportography, as advocated by Rousselot[8], facilitates the decision as to whether to use the portal or the splenic vein in establishing a shunt.

Follow-Up Care: In any given case where acute massive hemorrhage has been controlled by tamponage and where the patient has been successfully prepared for and carried through a portacaval shunt, we believe that we have extended life expectancy. By the very nature of the disease process, which encompasses an enormous number of variables, direct comparison with a control series of conservatively treated cases can often be challenged. It is a universally accepted clinical impression that hemorrhage from varices can initiate a chain of events that leads to rapid liver failure and death. Philosophically, any therapeutic mea-

TABLE V—EPISODIC STUPOR—60 CONSECUTIVE CASES
1956-1958

Portacaval Shunts	51		
Survived Operation	47		
Episodic Stupor	19		
Temporary	8	Associated Diabetes	0
		Associated Ascites	1
Prolonged	11	Associated Diabetes	3
		Associated Ascites	3
		Associated Diabetes & Ascites	3
No Episodic Stupor	28	Associated Diabetes	1 (mild)
		Associated Ascites	7 (mild)

sure that controls active homorrhage or prevents future hemorrhages should be of value, if, at the same time, the measure does not accelerate the basic disease process in the liver. Without intent to compare, Table IV will give some idea as to expected longevity following successful portacaval shunt; it includes patients who have had recurrence of bleeding, presumably as a result of a late failure of the shunt to reduce portal pressure to safe levels.

Episodic stupor (the so-called ammonia intoxication) has been advanced by the critics of portacaval shunting as an inherent danger of the procedure. This is true, but as our recognition and experience have been extended, the dangers of episodic stupor have diminished.

Uncontrolled, this complication has probably contributed in the past to a diminished life expectancy following portacaval shunt. However, with the advent of Neomycin and Bacitracin, administered orally in combination and in small doses on a long-term basis, patients have remained free of episodic stupor for as long as two years, despite continued high protein diets (Table V).

Summary: In summary, it is our current conviction that hemorrhage resulting from varices associated with portal hypertension arising from cirrhosis of the liver should be controlled immediately by balloon

tamponage of the esophageal varices. If hemorrhage is not controlled, immediate gastrotomy and ligature of the bleeding points should be undertaken. After a period of preparation on a controlled medical regimen, portacaval shunts should be performed on those patients who have the capacity to improve liver function if previously depressed, or sustain a high level of liver function if initially present. In those instances where a shunt cannot be performed because of portal or splenic vein thrombosis, or has failed, obliterative or excisional procedures should be considered.

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THERAPY OF MYASTHENIA GRAVIS*

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INTRODUCTION

MYASTHENIA gravis is characterized by weakness and excessive fatigue of striated muscle. The disease is not associated with specific primary changes in the central nervous system and for this reason it was named "bulbar palsy without anatomical findings", by Oppenheim. Structural changes, however, are found with some regularity in the thymus, which may persist without involution in adults or may even be enlarged; and in about 25 per cent of cases thymomas are found. In addition, lymphocytic infiltrations are found in striated muscle with no clear-cut relation to the degree of weakness. Lesions resembling myositis and true atrophy of muscles are rare and may represent a variant of the disease.

The main abnormality in myasthenia gravis is a disturbance in the transmission of the nerve impulse to the muscle for repetitive stimuli and particularly for maintained tetanic contraction. The cause of this disturbance is most likely a deficit in the acetylcholine metabolism at the neuromyal junction. This may be due to an excess of cholinesterase, the enzyme which hydrolyzes acetylcholine, though this has never been actually demonstrated. It is possible that in addition a conduction block exists in the endplate of the resting myasthenic muscle. The presence of curare-like blocking agents, circulating in the blood of patients suffering from myasthenia, has been postulated but is, as yet, unproven. It has been suggested that abnormal thymic tissue may be the source of this curare-like substance.

The distribution of the weakness in myasthenia gravis varies greatly. Any or all of the striated muscles may be involved in the course

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of the disease. Weakness of extraocular muscles with diplopia and ptosis is the most frequent initial sign and in some cases may be the only manifestation of the disease. In most cases other muscles supplied by cranial nerves are involved at one time or another. Facial weakness, dysarthria, weakness of muscles of mastication and deglutition are commonly found, often early in the disease. In other cases the illness may begin with weakness of muscles of the neck and shoulder girdle. Still other patients first notice weakness of hip muscles or of dorsiflexors of the foot and calf muscles. Dyspnea is rarely seen at the onset of the illness. When it occurs, especially combined with dysphagia, the prognosis is much more serious.

The degree of weakness may fluctuate considerably in individual muscles in the same patient and treatment may alleviate the weakness in some muscles but not in others. The extraocular muscles and the muscles of articulation are often resistant to drug treatment which corrects the weakness of extremity muscles and may remain weak when there is a complete remission of symptoms in other muscles. These facts and the high incidence of spontaneous remissions have to be considered in evaluating therapy.

The weakness of myasthenic muscles usually increases as the day wears on. In mild cases, rest alone may be sufficient for restitution of strength, but most patients require some form of drug therapy. Failure of vital functions, especially during a crisis, calls for additional measures, such as the use of oxygen, mechanical respirators, tube feeding and the correction of dehydration and electrolyte imbalance.

Short-Acting Drugs

Physostigmine, the antidote for curare, was used unsuccessfully by several investigators at the end of the 19th century. Mary Walker in 1934, using the drug for the same rationale, found striking, though not uniform improvement of myasthenic weakness following hypodermic injection of 1.0-1.25 mg. of physostigmine salicylate in one patient who was able to tolerate the side-effects (cardiovascular, respiratory and gastrointestinal) of the drug.

One of the important pharmacological properties of physostigmine is a strong but reversible inhibition of cholinesterase which lasts for several hours. Neostigmine, a synthetic physostigmine analogue, a relatively strong inhibitor of cholinesterase, was tried in the treatment of

myasthenia gravis in 1935 and was found to be more effective and less toxic than physostigmine. Neostigmine has, in addition, a direct stimulating effect on striated muscle. A systematic search for substances with anticholinesterase effect, which have also antimyasthenic properties, has led to the synthetization of a number of usable compounds. Most of these have been tried and discarded because they were less efficient or more toxic than neostigmine, which is still the most reliable drug for the treatment of myasthenia gravis. Two compounds recently produced which have been found to be of clinical value are pyridostigmine (Mestinon) which is related to neostigmine in structure and effect, and ambenonium chloride (Mytelase), a compound with a different molecule.

Neostigmine is available in two forms: as methylsulfate, usually in a solution 1:2000, for parenteral use and as hydrobromide for oral use (15 mg. tablets). In an untreated patient with moderately severe myasthenia, the subcutaneous injection of 1.0-1.5 mg. of neostigmine will bring relief of weakness within 10 to 30 minutes. The effect usually lasts for 3 to 4 hours with a rather quick "let-down" after this time. The ratio of oral to parenteral dosage of neostigmine is approximately 30:1 by weight. The onset of action of oral neostigmine is within 30 minutes; the effect lasts also for 3 or 4 hours. The average oral dose is 30 mg. or two tablets every 3 to 4 hours. In cases with severe weakness, 60 to 75 mg. may be required every 2 hours around the clock, and when dysphagia is present, this dose may have to be supplemented by parenteral medication before meals. Even larger amounts may have to be administered to patients with severe weakness.

Pyridostigmine (Mestinon Bromide) is available in solution, 2:1000, and in tablets of 60 mg. It is immediately comparable with and interchangeable for neostigmine at a ratio of 4:1 by weight. Its effect is similar to that of neostigmine. Some patients report a slightly longer duration of optimal activity with a less severe "let-down" at the end of a 3 or 4 hour period. Average and maximal dosages are about four times as great as for neostigmine. We have been unable to confirm the observation by some authors that pyridostigmine is more effective than neostigmine in correcting extraocular muscle weakness and dysarthria. Nor have we noted a longer effect of the drug at night. Side-effects, however, are less marked with pyridostigmine than with neostigmine in a number of patients.

Ambenonium chloride (Mytelase) is another clinically useful compound, different in its molecular structure from neostigmine, but with a comparable anticholinesterase effect. Its anti-curare activity is said to be two to three times that of neostigmine. The original impression, that its effect is of much longer duration than that of the other two compounds, has not been confirmed by our experience. It is available in 10 mg. and 25 mg. tablets. The dosage varies from 10 to 40 mg. every 3-4 hours. The drug is also available in solution for parenteral use.

Some toxic side-effects develop in most patients when they are given neostigmine therapy. With pyridostigmine and ambenonium the side-effects are usually, but not invariably, milder. The toxic side-effects of all three of these drugs are seldom of a serious nature in cases where small or moderately large amounts are required. Many patients develop a tolerance for the toxic side-effects of the cholinergic drugs, and do not require compensatory medication.

The side-effects most frequently encountered are referable to the gastrointestinal tract: abdominal cramps, increase in peristalsis, diarrhea, nausea and occasional vomiting. Next in frequency are signs of glandular hypersecretion, most commonly of the bronchial mucosa and salivary glands but also occasionally of the sweat and lacrimal glands. Bronchospasm and, in sensitive subjects, asthmatic attacks may occur. Tachycardia, commonly seen with physostigmine, is encountered rarely with neostigmine. In pharmacological terms, these side-effects are classified as "muscarinic" phenomena.

Another group of side-effects consists of excessive stimulation of striated muscle with resulting fascicular twitches, spasms of entire muscles, "freezing" of muscles, tremor and occasionally incoordination. These are "nicotinic" phenomena.

Finally a paradoxical curare-like effect with paralysis of muscles may occur after initial improvement of muscle strength when larger than therapeutic doses of neostigmine are administered.

The most severe form of reaction of anticholinesterase drugs, composed of all three elements but with muscarinic effects dominating the picture, is known as "cholinergic" crisis. This situation is a real emergency. Spasm of smooth muscle in the tracheo-bronchial tree and extreme oversecretion of mucus and saliva result in profound dyspnea. This may be associated with tachycardia and peripheral shock; in addition nausea, vomiting and violent abdominal cramps with diarrhea may

be present. In cases where dyspnea and muscle weakness are outstanding, this state may be mistaken for a myasthenic crisis. Attempts at treatment with additional cholinergic medication may be fatal.

The prevention of muscarinic side-effects consists in administration of atropine sulfate, 0.3 to 0.6 mg. in milder cases and 1.0 to 2.0 mg. in severe cases. This dose may be repeated (even by intravenous injections) every hour in a crisis. Small amounts of atropine (0.3 to 0.6 mg.) should be given with anticholinesterase drugs to all patients when treatment is started. In some instances atropine should even be given 20 to 30 minutes before each dose. Some patients prefer tincture of belladonna because the dosage is more easily adjustable. Synthetic analogues of atropine have been found useful especially with patients who have become habituated to atropine. The "nicotinic" phenomena are not controlled by drugs of the atropine series and the use of these drugs is not without some inherent danger. The effect on respiratory weakness with inability to cough may be unfavorable. Increase in viscosity of bronchial secretion may lead to additional respiratory embarrassment. In this situation tracheal suction should be used. Plugs of inspissated dried mucus may require bronchoscopy for removal. With large doses of atropine, which we have to use in many cases, confusion, tachycardia and an elevation of temperature may occur. Nevertheless, without atropine, correction of weakness by anticholinesterase drugs would be incomplete in many cases and impossible in some. The danger of masking an impending cholinergic crisis by atropine has in our opinion been greatly over-emphasized.

Many patients gradually lose the extreme sensitivity to the muscarinic side-effects of neostigmine and the other drugs, require atropine less often or not at all and may be able to protect themselves against the gastrointestinal overstimulation by taking the medicine with meals or with small amounts of food at other times.

Edrophonium chloride (Tensilon) is an anti-curare compound with an anticholinesterase action of brief duration. It is used as a diagnostic rather than therapeutic agent. Myasthenic weakness in an untreated patient may be strikingly relieved in 30 to 60 seconds after intravenous injection of 10 mg. of the drug. The Tensilon test has also been recommended for the differential diagnosis of myasthenic and cholinergic weakness. Brief improvement may occur when Tensilon is administered to a patient who is receiving less than the optimal dose of neostig-

mine or other anticholinesterases. A transient increase in weakness and in the muscarinic side-effects should be expected in patients who have received too much of the anticholinergic drugs. Because of the evanescent effect of Tensilon, there is little or no danger. We have found the test misleading at times. Improvement may occur in some muscles and worsening in others, probably due to the uneven distribution of weakness and drug responsiveness of different muscles in more severe cases.

Evaluation of Conventional Drug Therapy: Patients with mild or moderately severe but stable myasthenia may benefit greatly by treatment with neostigmine and other short-acting drugs and are able to lead fairly normal active lives. Many of these patients learn to adjust the dosage of medicine to the varying daily needs, adding or omitting according to anticipated activities or the fatigue they experience. A small number of these patients will have a spontaneous remission. In some patients strength is not fully restored by these drugs. The improvement, for which they pay with some discomfort, is followed within 3 or 4 hours by a marked let-down. In more severe cases the effect of the drug begins to disappear after 2 hours. Many patients take medication at intervals through the night or else are unable to get up in the morning or to swallow the first morning dose.

One of our patients, a school boy of 13, known to us since the age of 13 months, requires medication varying from 30 to 45 mg. every two hours from 6 a.m. to 10 p.m. When this regime is strictly maintained, he is able to study and play normally in spite of an almost intractable external ophthalmoplegia and facial weakness. If medication is delayed beyond the two hour period, he experiences general weakness, dysphagia, dysarthria and at times dyspnea. Other patients with similar rigid drug requirements hold jobs or keep house for large families.

Long-Acting Drugs

For the group of patients who can be kept out of invalidism, the uneven maintenance of strength due to the short action of the conventional drugs is a severe handicap. For this reason, we and others have tried long-acting compounds in the treatment of myasthenic patients.

Alkyl Phosphates: A group of highly toxic compounds with a profound anticholinesterase effect have been synthesized in recent

years for use as insecticides and potential agents for chemical warfare. In contrast to physostigmine and neostigmine, the alkyl phosphates inhibit cholinesterase irreversibly. Several of these substances have an anti-myasthenic effect of long duration, but, with one exception, they are of limited use because of their toxic side-effects, which include several central nervous system manifestations (insomnia, over-activity and seizures). In addition, the range between the therapeutic and toxic doses is narrow. One of these substances, octamethyl pyrophosphoramide (OMPA) is stable in aqueous solution and relatively non-toxic. Its therapeutic effects are similar to those of neostigmine as are also its muscarinic and nicotinic side-effects. Atropine is the main antidote for the muscarinic effects. The anticholinesterase action of a therapeutic dose lasts for several weeks, which is presumably the time necessary for the body to resynthesize cholinesterase, and for this reason, great care has to be taken to avoid overdosage. When fully adjusted to the drug, patients may be maintained on 15 to 20 mg. twice a day. On this dosage control of myasthenic weakness is achieved without the fluctuations which occur with the administration of short-acting compounds. The degree of correction of weakness with OMPA does not, however, exceed that which can be obtained with neostigmine. The manufacture of the drug has been discontinued because of its great toxicity during the process of purification for clinical purposes. In recent years it was found that certain oximes may be used for the reactivation of cholinesterase which has been inhibited by alkyl phosphates. This might have a direct bearing on the future use of these substances even though an antidote for OMPA has not yet been found.

BC Substances: A very promising new approach to the treatment of myasthenia gravis is the introduction of polymethylene-linked double molecules of neostigmine and pyridostigmine. They are reversible anticholinesterase compounds with intermediate duration of effect. We have used BC-51, a substance with a double pyridostigmine molecule. Its chemical formula is: Hexamethylene-Bis-(N-Methylcarbaminoyl-1-Methyl-3-Oxypyridium Bromide). The onset of the effect of this compound is delayed for about 72 hours. Its inhibitory action on cholinesterase subsides in a similar period of time. Alkyl phosphates by comparison have an action extending over weeks. Toxic side-effects of BC-51 so far have been mild in most cases.

In order to avoid overdosage, patients treated with long-acting drugs

should be given suboptimal amounts with supplementary doses of short-acting drugs.

Myasthenic Crisis

Despite an apparently rational therapy, patients die of myasthenia gravis. Death from acute respiratory failure may occur suddenly at a time of relative well-being or even during an apparent remission. In other cases death may be due to insufficient therapy, to overdosage of medication or to complete failure of therapeutic agents.

A respiratory crisis may be preceded by repeated brief episodes of dyspnea with spontaneous recovery. Other premonitory signs are anxiety, episodes of confusion, irritability or irrational behavior. Determination of arterial oxygen or CO_2 tension at these times may show moderate anoxia or hypercapnia. The treatment for these episodes is a parenteral injection of neostigmine. Oxygen should be available. Sedatives are contraindicated at this time for patients who are not in a respirator.

In most cases a crisis is preceded by progressive weakness in spite of the administration of increasingly large amounts of anti-myasthenic medication. Refractoriness to drugs is often precipitated by an upper respiratory infection.

When these conditions occur, a crisis must be expected. A tank-type respirator, tracheotomy set, oxygen and suction equipment should be kept available. If time permits, an elective tracheotomy should be performed. Following tracheotomy the patient is placed in the respirator and oxygen administered as needed. Drugs are withheld, atropine administered judiciously to keep the airway dry, and suction is employed to keep it open. For the average adult the respirator is set for a negative pressure of 15 pounds (and if needed a positive pressure of 5 pounds) per stroke at the rate of 16 strokes per minute. This may be modified in order to avoid overventilation and alkalosis. Electrolyte balance is maintained by parenteral infusions, especially in patients who are dehydrated due to dysphagia or as a result of diarrhea secondary to the toxic effects of the drugs. Sedatives may be administered and morphine may be beneficial while respiration is maintained mechanically. Antibiotics in doses sufficient to prevent pneumonia should be given. After a few days, it is usually possible to stop the respirator temporarily without removing the patient from it and later the patient can be

allowed out of the respirator for increasing periods as tolerated.

In cases where the muscarinic side-effects of anticholinergic drugs are outstanding, they should be discontinued for at least several days. In some cases, however, small amounts may be used in order to permit the patient to communicate, cough and swallow. A period of relative or complete abstinence from the drugs may lead to a return of sensitivity to medication, usually at much lower levels than before the crisis. In some cases a remission may follow a crisis.

THYMECTOMY

Hyperplasia of the thymus and thymic tumors is found in a large percentage of cases. Figures from several large clinics vary from 15 to 25 per cent. There is at this time no convincing evidence of a causal relationship between these abnormalities and myasthenia gravis. The high incidence of these findings certainly needs explanation.

The evaluation of the results of surgical removal of thymic tissue for myasthenia gravis is difficult. Various factors must be considered. They are, age and sex of the patient, duration and severity of the illness and the presence or absence of a thymoma. The results from the several clinics, where large series of thymectomies and thymomectomies have been performed, vary considerably. It is, however, generally accepted that the presence of a thymoma carries an unfavorable prognosis. This is true for operated as well as unoperated patients and is in keeping with the fact that thymoma is statistically found in the older age groups and is usually associated with a more severe form of the illness. Mortality for patients with thymoma is said to be about 66 per cent for the operated as well as the unoperated groups.

From recent surveys it would appear that surgical results are more favorable in younger patients who have had the illness for a few years and whose requirements for anticholinesterase drugs have been low. This includes, of course, the patients with the milder form of myasthenia. Young women (15 to 45 years of age) are considered by one group of workers to benefit mostly by thymectomy. From other figures it would appear that, if properly selected, young men may equally benefit by thymectomy.

The beneficial results of operation, full and partial remissions, occur usually after many months and hardly ever immediately after operation. It should also be stressed that recurrences of myasthenia occur after

surgical treatment and after spontaneous remissions with fatal outcome in both groups.

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MANAGEMENT OF PERIPHERAL VASCULAR DISEASE

*Transcription of a Panel Meeting on Therapeutics**

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MODERATOR IRVING S. WRIGHT: In considering how to present the management of peripheral vascular disease, it seemed clear that there were many questions which should be discussed by the panel. We shall try to do this in an informal manner. When confronted with a person with occlusive vascular disease, we must first ask ourselves what we wish to accomplish. In order to determine this we must establish a diagnosis. We must determine whether there is an arterial or a venous occlusion. Sometimes both arteries and veins are involved. Was the occlusion gradual or sudden? Was it due to atherosclerosis, thromboangiitis obliterans, Raynaud's phenomenon, or an embolic closure? Was it due to thrombophlebitis with reflex arterial spasm? Was it due to external pressure such as a cervical rib or a hyperabduction syndrome, or a tumor? There are many other possibilities to be considered.

We must then determine the status of the circulation. Is there moderate ischemia, producing intermittent claudication, is it more serious, with impending gangrene, or is there actual gangrene present? Is there infection? Is edema present? We must search for underlying diseases which must be treated. Does the patient have polycythemia vera which tends to increase the likelihood of thrombosis and hemorrhage in both arterial and venous trees, thromboangiitis obliterans, or diabetes mellitus? Does he have atrial fibrillation with mural thrombi and possible embolization? The treatment to be considered must be physiologically sound.

Even such simple questions as the advisability of rest for the affected part are at present subject to a critical re-evaluation. Dr. Foley, do you place the patient at complete rest? In what position should the foot be maintained? How long should the rest continue? How do you determine when to allow the patient to be active? Does weight-bearing do harm or good? Will you answer a few of these questions?

DR. WILLIAM T. FOLEY: I think the key to the answer is contained in your own statement, made a moment ago, when you said that any treatment must be based on sound physiological grounds. What are we trying to do in the patient with arterial occlusion? Of course we are trying to increase the blood flow. On the one hand, inactivity may have the beneficial effect of placing the part at rest and we know that any pathological lesion heals better if it is at rest. Even when one has a sore finger, it heals better if one puts it in a splint, or if a lung has a lesion such as tuberculosis, we put the patient at rest and minimize the excur-

sion of the lung by pneumothorax or some such measure. On the other hand, resting an extremity leads to disuse and disuse in all living things is associated with atrophy. When in bed, the skin, bone and blood vessels atrophy. In a patient with normal circulation, when confined to bed, the nails cease growing, the hair does not grow, the bones lose calcium, the vessels themselves shrink and one gets decreased blood flow. Where is the compromise between these two factors, rest and use?

I think if one can put the afflicted tissue itself at rest by using a bandage or a splint, and can get the patient up and walking, one then has the optimum physiological urge for blood flow. We find that a patient at rest, compared to a patient who walks, say, 100 yards, has a considerably reduced blood flow; the rate of blood flow down the iliac artery can be augmented more than ten times if he walks 100 yards. There is no modality among all of our therapeutic facilities, either sympathectomy or sympathetic block or drugs, or any other measure that can increase the blood flow as markedly as exercise does.

MODERATOR WRIGHT: *Dr. Foley, does the presence of infection with drainage of purulent discharge influence you?*

DR. FOLEY: I think it does, definitely. If one has a spreading gangrene, then the motion of the part involved in having the patient walk may tend to spread the lesion and for that reason we have been hesitant to have these patients walk, but if we have a demarcated gangrene, then we do have the patients get up.

MODERATOR WRIGHT: *Bear weight?*

DR. FOLEY: Bear weight on the foot.

MODERATOR WRIGHT: Dr. Lord!

DR. JERE W. LORD, JR.: I should like to refer to a point that Dr. Foley alluded to earlier. At first there is acute deprivation of arterial flow to the lower extremity. Certainly at the very beginning, other than to establish the cause of this deprivation, one should use rest and should use it wisely. It has been pointed out many times that one of the harmful things that some of us might do is to elevate the part, to put it at rest on a pillow. It has been brought out that gravity is one of the best friends we have to encourage blood flow to that part. Therefore to obtain the effect of gravity, it would require lowering the part deprived of blood. It is better to raise the head of the bed on blocks rather than to gatch the bed or to put it in mid-Fowlers position. Raising the head of the bed 6 or 8 inches brings the heart level with the toes and gradually

encourages the blood to flow through the collateral circulation. A much better method, if one has such equipment available, is the properly operated oscillating bed. When handled properly, so the foot of the bed is lower than the head during part of the cycle, it is a useful device. The poorly operated oscillating bed may be worse than not using it at all.

MODERATOR WRIGHT: We are still seeing patients, and Dr. Foley currently has one under his care, who have a painful foot due to a sudden arterial occlusion. Dr. Foley found that the patient's doctor had elevated the foot on a pillow. For this condition this is the worst sort of treatment. It is the opposite of what should be done. With arterial blockage, the foot should be kept below the heart level to encourage the flow of blood to the extremity. On the other hand, if you have good arterial circulation and you have venous obstruction with swelling of the foot, elevation of the foot of the bed is indicated. This is just common sense. It is just a physiological principle. The oscillating bed is the best form of therapy that we have for this problem. It not only results in flow of blood, but it also aids in retaining calcium in the bones and, to a remarkable degree, gives the person passive exercise 24 hours a day, which is very important in the care of these patients.

The next question deals with the use of heat. Heat has been used very improperly. We have now seen nearly 100 patients who have been badly burned, some of them developing gangrene and in some amputation has been unavoidable due to misapplication of diathermy, infra red lamps, hot water bags or other forms of heat directly to the foot. This is especially serious in patients with diabetes where a peripheral neuritis has resulted in anesthesia of the foot. These patients are often not aware that the foot is being burned until very serious damage has been done.

Dr. Mendlowitz, how do you use heat, or do you use it?

DR. MILTON MENDLOWITZ: We do not use direct heat at all in the treatment of a patient with occlusive arterial disease. There is reason, in some cases, to use what is called reflex heat. This is heat applied not to the affected limb itself but to the trunk or to an arm in order to produce reflex vasodilatation and get whatever inhibition of sympathetic nerve discharge can be obtained in this way. This can be done by the use of a cradle baker over the trunk, for example. It is only useful where some degree of neurogenic vasospasm can be demonstrated, and in acute occlusion that is usually in the beginning or immediately after the event

has taken place. In the later phases of this condition, vasospasm, if it is present at all, is not the important factor that it is in the early stage of the embolization.

MODERATOR WRIGHT: *Are there any further comments on the question of heat, Dr. Foley?*

DR. FOLEY: A warm tub bath with the temperature of the water carefully controlled so that it is not above body temperature is a very valuable adjunct.

MODERATOR WRIGHT: We are now going to talk about the sympathetic nervous system. This can be divided into three phases: First, there is the question of sympathetic blocks. Should sympathetic blocks be used or not used for an acute occlusion? What are the indications and the contraindications? The second part is the question of surgical sympathectomy, and the third part, the question of the use of drugs which attempt to produce a non-surgical sympathectomy.

Dr. Lord, will you open the discussion of the use and the misuse of sympathetic blocks?

DR. LORD: In any patient who has acute arterial occlusion, the first thing to do is to determine whether one can relieve the occlusion, whether embolic or thrombotic or traumatic in origin. If we assume that we cannot relieve the obstruction by prompt surgical means, then intervention on the sympathetic system must be considered. It may be employed in two ways with different purposes in mind. One will be to try to get rid of all vasospasm of that extremity, realizing that the usual medication such as procaine or xylocaine, will last only a few hours. The second purpose is to use it as a diagnostic procedure as a prelude to sympathectomy.

If, when the patient is first seen, you cannot do a direct surgical procedure on the occluded vessel, then a sympathetic nerve block may effect an immediate break of the vasospasm and anticoagulants can be started. After the anticoagulant is started, however, I personally feel extremely reluctant about carrying out further blocks on the sympathetics because if hemorrhage occurs, it may not be recognized for some time or if recognized, it may be difficult to control. We will then use the reflex heat which Dr. Mendlowitz has recommended.

MODERATOR WRIGHT: *Dr. Lord, is there any evidence that keeping a patient under reflex heat will prolong the effect of the block as compared with omitting the use of heat?*

DR. LORD: I don't know of any such evidence. On the other hand, it seems to me that, properly applied, reflex heat will do just about everything that a paravertebral block will do. The only drawback is that the block which gives a complete and immediate response is difficult to continue every six to eight hours, both for the patient and the physician, whereas the reflex heat can be carried out most satisfactorily by the nursing staff.

MODERATOR WRIGHT: *We will discuss sympathectomy a bit later but I have another question. It has been stated that the vasodilatation which takes place as the result of sympathectomy is almost entirely limited to the superficial vessels and that the deep vessels are not dilated. If this is true for sympathectomy, would it not be true for a sympathetic block and would this factor influence the selection of the cases in which you would use block?*

DR. LORD: In the acute stage I think we are all concerned with the integrity of the skin and hope to save the limb. We are not concerned about intermittent claudication because, for the moment, that has not even become a problem. Therefore I think the block or sympathectomy may be indicated to try to save the limb in the acute stage of arterial insufficiency. There are divergent opinions between medical men and surgeons with regard to the value of sympathectomy for intermittent claudication. I am one of the group which holds that there is no evidence that interruption of the sympathetic nervous system improves the blood flow to the muscle. I know of no clinical or experimental evidence that is incontrovertible, therefore I do not perform a lumbar sympathectomy on a patient who has intermittent claudication as his only symptom.

MODERATOR WRIGHT: *Dr. Mendlowitz, what do you do for your patient?*

DR. MENDLOWITZ: If there is occlusion of a large vessel and demonstrable vasospasm, and by that I mean that one can release this vasospasm and produce appreciable change in the temperature of the skin, or if other criteria for measuring blood flow, such as the plethysmograph, calorimeter or just palpation with the hand, indicate that there is vasospasm and this is an acute situation, then I think that sympathetic blockade is indicated to tide the patient over and save as much of the skin and of the limb as it is possible to save. I think that at this point the question could be interjected as to whether one could get more

of an effect in terms of increased blood flow by such a procedure as the intra-arterial injection of Priscoline, which is believed to act not only on the sympathetic nerves but also by dilating the capillaries themselves.

MODERATOR WRIGHT: *Dr. Mendlowitz, you have asked a question. Can you answer it?*

DR. MENDLOWITZ: I can only say that frequently one is faced with a situation in peripheral vascular disease in which the skin figuratively hangs in the balance and may be permanently compromised, where the femoral artery is patent, yet there is no occlusion above it. In such an instance, regardless of additional measures resorted to, such as sympathetic blockade, it is feasible to inject intra-arterially something in the nature of Priscoline, provided one is alert to the rare case in which Priscoline can *produce* an arterial thrombosis.

MODERATOR WRIGHT: *We have not opened the discussion of drugs yet, but you have mentioned Priscoline. What about histamine? It has been advocated by some workers.*

DR. MENDLOWITZ: That involves a more elaborate technique and requires setting up an arterial inflow system. It is not, in my opinion, very practical unless you have a rather elaborate team with continuous nursing and medical coverage.

MODERATOR WRIGHT: We will get to that a little later.

Dr. Foley, would you comment on sympathetic blocks.

DR. FOLEY: I think sympathetic block has the great advantage of pinpointing the vascular dilatation. One can limit it to the affected limb whereas many of our other measures are apt to produce dilatation in all four limbs and also in the trunk. It has the disadvantage that it should not be done if the patient is receiving anticoagulants.

Usually equally good results can be obtained with simpler measures such as sub-lingual nitroglycerin. When simpler measures fail, then we would use the block.

MODERATOR WRIGHT: *Dr. Lazzarini, do you have any comment?*

DR. ABEL A. LAZZARINI, JR.: Just to say that the sympathetic block has the disadvantage of lasting only a few hours and then it must be repeated in order to observe any appreciable effects.

MODERATOR WRIGHT: I think there are two points that we should emphasize. One is that if you are going to do sympathetic blocks, you should be prepared to do several, at six or eight hour intervals, in the

event that the first one does not succeed. I have seen some patients in whom the effect was negative after the first one but became pronounced after the second or third.

Secondly, the opinion has been expressed that it was unwise to do sympathetic blocks when a patient is on anticoagulant therapy. It is true that there have been several deaths reported as the result of this approach. However, just for the sake of being the devil's advocate, I would like to record that there are a number of workers who feel that this danger has been grossly over-stressed and that actually, if the block is done carefully and not in a traumatic way, it can be relatively free from danger.

Dr. Gerald Pratt has reported 2116 blocks in 554 patients on anticoagulants without serious hemorrhage. It is his belief that serious hemorrhages are not due to simple puncture but to faulty technique resulting in torn vascular walls. This presents the other side of the coin.

Now we will discuss sympathectomy, a more drastic procedure. Some patients are not in very good shape for such an operation, yet this procedure must be considered. Dr. Lord, will you open this discussion?

DR. LORD. There are three situations in which sympathectomy is well worth considering. First, in the individual who has the acute occlusive lesion but is not amenable to direct arterial surgery after a block has produced marked improvement in a foot which was in jeopardy and in whom the symptoms have returned after the block wore off. If there is no contraindication to sympathectomy, it may then be valuable in the acute stage. I have had a number of patients of that type.

The second is in the individual who has had excellent medical care, in an attempt to improve a chronically deficient circulation to the limb, and yet the desired result has not been achieved; when there is still cyanosis of toes, rest pain, in addition to the original problem,—a patient who is not symptom free and in whom amputation is not indicated. In such a case sympathectomy may help after resting for vasomotor tone. Dr. Mendlowitz referred to this as "vasospasm", but I prefer to use the term vasomotor tone since some of these patients manifest a degree of activity of the sympathetic nervous system which is subtle and should be studied in a constant temperature room under reduced temperature. Several methods can be used to break the tone

such as paravertebral block or reflex heat. The temperature of the skin of the toes should then be determined and should there be evidence of vasomotor tone, a sympathectomy may be of value.

Finally, sympathectomy may be helpful, after medical therapy has been proved to be inadequate, in those patients manifesting such functional disturbances as Raynaud's disease, reflex pneumatic hammer disease, the so-called reflex motor dystrophy.

MODERATOR WRIGHT: *Dr. Lord, I would like to have your opinion regarding the value of sympathectomy in the treatment of intermittent claudication.*

DR. LORD: Not infrequently one sees patients who have intermittent claudication and no other symptom such as rest pain, gangrene, or ulceration. They walk one or two blocks and have a cramp and stop, rest, walk again,—pain comes on walking and goes away with rest. Such a patient is often seen in consultation early in the course of his trouble. He probably suffered thrombosis of the femoral artery in the adductor canal. If early in his trouble a sympathectomy is performed, the walking distance will improve in a matter of weeks or months and surgery will take the credit. Such a patient, treated by medical management, will do equally as well as one treated by sympathectomy and in some instances will do better because the sympathectomy may take some of the blood away from the calf muscles and divert it to the superficial tissues. Other patients who have chronic intermittent claudication but who have not followed good medical advice may undergo lumbar sympathectomy. If, following that procedure, they follow and adhere to good medical measures, they will do better. My own experience, in private practice and on the Fourth Division of Bellevue Hospital, is that no patient with intermittent claudication has ever been helped by lumbar sympathectomy who has previously been on good medical regimen.

MODERATOR WRIGHT: *Dr. Mendlowitz, do you advise sympathectomy in the treatment of intermittent claudication?*

DR. MENDLOWITZ: No.

MODERATOR WRIGHT: *Dr. Foley, do you use it in the treatment of intermittent claudication?*

DR. FOLEY: No, I do not but may I just point out that I think Dr. Lord is a most unusual surgeon. He is a student of vascular disease and approaches this problem from a broad point of view. Many surgeons approach the sympathetic nervous system as they would the appendix

event that the first one does not succeed. I have seen some patients in whom the effect was negative after the first one but became pronounced after the second or third.

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Now we will discuss sympathectomy, a more drastic procedure. Some patients are not in very good shape for such an operation, yet this procedure must be considered. Dr. Lord, will you open this discussion?

DR. LORD: There are three situations in which sympathectomy is well worth considering. First, in the individual who has the acute occlusive lesion but is not amenable to direct arterial surgery after a block has produced marked improvement in a foot which was in jeopardy and in whom the symptoms have returned after the block wore off. If there is no contraindication to sympathectomy, it may then be valuable in the acute stage. I have had a number of patients of that type.

The second is in the individual who has had excellent medical care, in an attempt to improve a chronically deficient circulation to the limb, and yet the desired result has not been achieved; when there is still cyanosis of toes, rest pain, in addition to the original problem,—a patient who is not symptom free and in whom amputation is not indicated. In such a case sympathectomy may help after testing for vasomotor tone. Dr. Mendlowitz referred to this as "vasospasm", but I prefer to use the term vasomotor tone since some of these patients manifest a degree of activity of the sympathetic nervous system which is subtle and should be studied in a constant temperature room under reduced temperature. Several methods can be used to break the tone

such as paravertebral block or reflex heat. The temperature of the skin of the toes should then be determined and should there be evidence of vasomotor tone, a sympathectomy may be of value.

Finally, sympathectomy may be helpful, after medical therapy has been proved to be inadequate, in those patients manifesting such functional disturbances as Raynaud's disease, reflex pneumatic hammer disease, the so-called reflex motor dystrophy.

MODERATOR WRIGHT: *Dr. Lord, I would like to have your opinion regarding the value of sympathectomy in the treatment of intermittent claudication.*

DR. LORD: Not infrequently one sees patients who have intermittent claudication and no other symptom such as rest pain, gangrene, or ulceration. They walk one or two blocks and have a cramp and stop, rest, walk again,—pain comes on walking and goes away with rest. Such a patient is often seen in consultation early in the course of his trouble. He probably suffered thrombosis of the femoral artery in the adductor canal. If early in his trouble a sympathectomy is performed, the walking distance will improve in a matter of weeks or months and surgery will take the credit. Such a patient, treated by medical management, will do equally as well as one treated by sympathectomy and in some instances will do better because the sympathectomy may take some of the blood away from the calf muscles and divert it to the superficial tissues. Other patients who have chronic intermittent claudication but who have not followed good medical advice may undergo lumbar sympathectomy. If, following that procedure, they follow and adhere to good medical measures, they will do better. My own experience, in private practice and on the Fourth Division of Bellevue Hospital, is that no patient with intermittent claudication has ever been helped by lumbar sympathectomy who has previously been on good medical regimen.

MODERATOR WRIGHT: *Dr. Mendlowitz, do you advise sympathectomy in the treatment of intermittent claudication?*

DR. MENDLOWITZ: No.

MODERATOR WRIGHT: *Dr. Foley, do you use it in the treatment of intermittent claudication?*

DR. FOLEY: No, I do not but may I just point out that I think Dr. Lord is a most unusual surgeon. He is a student of vascular disease and approaches this problem from a broad point of view. Many surgeons approach the sympathetic nervous system as they would the appendix

or the tonsils,—the indication for removal is because it is there. This may be a harsh statement but we have seen hundreds of people who were subjected to sympathectomy for no apparent good reason. As Dr. Lord's studies have pointed out, the operation is not warranted in most cases of intermittent claudication.

MODERATOR WRIGHT: *Dr. Lazzarini, any comments?*

DR. LAZZARINI: No.

MODERATOR WRIGHT: It is bad enough to do a sympathectomy where it is not indicated, but it is even worse to do a sympathectomy and permit the patient to continue to smoke. Unfortunately this is a common situation. The surgeon does a sympathectomy without insisting that the patient stop smoking. Some of these patients have the feeling that they are protected because of the sympathectomy. Therefore they continue to smoke, despite the advice of other physicians.

Many of these patients have arterial occlusion because of an embolus, often released from a heart in fibrillation. This complication may involve any organ. It must be decided whether or not an attempt should be made to remove the occlusion by surgery. If the decision is for surgery, it should be acted upon promptly.

Dr. Lord, how do you decide on which cases you will attempt an embolectomy?

DR. LORD: I think this is the same problem that we face so often in the practice of the various branches of medicine and surgery. If we could make and follow hard and fast rules, the problem would be much simpler. One has to select,—select that therapy, whether medical or surgical, which is most appropriate for a particular patient, or conversely, select only those patients who are likely to benefit from a specific form of treatment. That selection is often a difficult decision to make. In a general way the following has been our experience: I have yet to do my first embolectomy in the upper extremity. We have seen quite a number of patients who, we believe, had a bona fide embolus to the subclavian, the auxiliary, the brachial artery or below and none of those patients has lost any tissue when treated medically by the means outlined earlier. I have heard of individuals whose hand has gone on to gangrene and I have heard of other surgeons who believe that they have saved an upper extremity by embolectomy. The lower extremity is quite a different problem. I believe the following to be correct: Any saddle embolus, unless clear-cut contraindication exists, should be treated

immediately by surgery.

MODERATOR WRIGHT: *This is at the lower end of the aorta?*

DR. LORD: At the bifurcation of the aorta, embolectomy should be done promptly. Other than getting the patient to the hospital, relieving pain, and treating the heart as best one can, one should operate as soon as possible. Nothing should be done before operation to determine what the effect of a paravertebral block might be.

When one has the same condition at the bifurcation of the common iliac or the bifurcation of the common femoral, prompt embolectomy is mandatory. When embolism occurs lower in the extremity, in the superficial femoral or popliteal arteries, then evaluation of the situation in the individual patient must be observed. I personally have never done a popliteal embolectomy. I do not believe we could ever have helped any patient we have seen. That is not the experience of a number of surgeons. They believe popliteal embolectomy may be strongly indicated. In some instances it may be so. Usually I have operated on the lower abdominal aorta and on the major arteries of the upper thigh and have been conservative elsewhere.

MODERATOR WRIGHT: *Dr. Foley, you have seen many patients with emboli in your day. Do you have further comments?*

DR. FOLEY: I agree completely. I would not change a word.

MODERATOR WRIGHT: *Dr. Mendlowitz!*

DR. MENDLOWITZ: I agree.

MODERATOR WRIGHT: *Dr. Lazzarini!*

DR. LAZZARINI: I agree.

MODERATOR WRIGHT: I agree, too. This is a sound way to approach this situation. Now to consider the problem of small vessels. I have seen emboli removed from the popliteal artery, not by Dr. Lord, but by others, only to have the vessel thrombose again rather promptly. In addition to the embolus or thrombosis with which the patient started, you have traumatized tissue. The circulation of the peripheral and collateral vessels has been interrupted and the operation has actually done more harm than good.

We will now discuss grafts. Dr. Lazzarini has, in recent years, been studying the problem of grafts. We shall ask him to open the discussion on this subject.

DR. LAZZARINI: I think that a summary of the problem of vascular grafting lies in the answers to two main questions. The first question is:

What type of graft is to be used? The second: In what type of patient should the graft be done?

Regarding the type of graft to be used, considerable study has been devoted in recent years to the possibility of using artificial prosthetic replacements of blood vessels, in other words, man-made blood vessels prepared and fashioned in the operating room. The reason for these studies has been the increasing difficulties in securing arterial homografts to be used in vascular surgery, namely, obtaining the proper donor at the proper time and the problem of preserving and maintaining adequate supplies in a blood vessel bank at all times.

A number of blood vessel banks have been established in many parts of the country during the past few years. It has been determined that the optimum age for donors of blood vessel grafts is between 15 and 35 years. These grafts should be taken, with or without sterile precautions, from patients who die of a known, non-transmissible disease. The main problem, of course, has been the question of the practicability of the technique, particularly in small communities.

In recent years considerable experience has accumulated in the use of grafts taken without sterile precautions and that have been sterilized by chemical or physical means in the laboratory and then preserved by various methods. These methods are, in general: freeze-drying techniques, quick freezing or preservation in a nutrient at 4° C. However, the problem of obtaining a sufficient number of donors' vessels of appropriate size at a given time is still present. Certainly the cooperation of the pathologists has helped a great deal but there are many places where these services are not available. It is for this reason that there is great interest in studying and experimenting with plastic prostheses. These are sheets or tubes of different kinds of plastic materials in the form of woven fabrics. These materials can be fashioned to proper size and shape and, after being sterilized just before use, can be implanted at any time. This method has considerable practical advantages over the use of natural prostheses such as homografts.

With natural prostheses, the autografts are taken from and transplanted into the same individual. The vessel is usually a vein graft and this procedure has proved very satisfactory in peripheral arterial disease. In the past few years considerable clinical experience has been obtained in the use of homografts, grafts taken from individuals of the same species. When used in peripheral vessels, however, the long-term results

have not been satisfactory. Finally, heterografts, or grafts taken from individuals of different species, for replacement of central or peripheral vessels have not been successful as yet. Although the practicability of using grafts from the animal kingdom should certainly be investigated further, with the exception of autografts, natural and plastic prostheses are at present not satisfactory in the surgical management of peripheral vascular diseases.

MODERATOR WRIGHT: *To which vessels do you refer; how large or how small a vessel is suitable for grafting?*

DR. LAZZARINI: The main surgical experience has been with replacement in the thoracic and abdominal aorta. The smaller the size of the vessels the more difficult it is to obtain a permanent satisfactory result. Vessels smaller than the popliteal arteries are usually unsuitable for grafting, not only because of their size but also because of the likelihood of extension of the disease.

MODERATOR WRIGHT: *Are there any members of the panel who wish to add or take issue with this statement? Dr. Lazzarini has made a very sound statement on the technique of vascular grafting. The use of grafts is increasing, not only here but throughout the world. Another decade will probably show marked improvement in techniques and application.*

Vasodilating drugs: We cannot discuss every drug that has been used as a vasodilator. Merely listing them would take too long. Among those more commonly used are Priscoline, Roniacol, TEAC, alcohol, papaverine, procaine, Dibenzaline, histamine, etc.

I shall ask Dr. Mendlowitz to outline the broad principles underlying the current use of vasodilators having a general systemic effect in the treatment of arterial occlusion in the leg.

DR. MENDLOWITZ: One general principle to emphasize is that most vasodilators in current use are effective in the skin circulation. Very few vasodilators that I know of are demonstrably effective, despite the claims, in the deeper circulation. Therefore if one uses vasodilators with the intention of affecting the deeper circulation, that is, the circulation in muscle, or specifically for intermittent claudication, then one is not likely to be very successful. It should be remembered that intermittent claudication tends to improve spontaneously, especially after an acute event such as an acute occlusion.

For intermittent claudication, the logical type of vasodilator to use is one which, in addition to having its effect on the sympathetic nervous

system, also has an effect on the capillaries, a direct effect in dilating capillaries in addition perhaps to relaxing the smooth muscle of blood vessels. Priscoline and histamine are in this class and are widely used for this reason in peripheral vascular disease. I must confess that when it is used *orally* I am not at all convinced that its effect is demonstrable except in a rather small percentage of cases, despite the fact that we always use these drugs and despite the fact that I am also convinced that they are of some value. This is a very vague statement and I am afraid I cannot document it by data because it is based purely on clinical impression. However, such data as are available in the literature indicate that drugs which act both on the capillaries and on the sympathetic nervous system are apt to be more effective than those which act on the sympathetic nervous system alone, especially if one is interested in treating a process which is compromising the skin circulation.

As far as general vasodilators are concerned, they all have the defect which Dr. Foley pointed out, which is that they dilate all the blood vessels instead of confining the vasodilatation to the blood vessels which are specifically involved in a single extremity. For that reason, efforts directed at the limb by means of intra-arterial medication sometimes have a use.

MODERATOR WRIGHT: *Someone in the audience has raised the following question: What is the opinion of the panel regarding histamine infusions in the treatment of arterial occlusion? I am going to ask Dr. Foley to answer this first because several years ago he was assigned the task of analyzing this problem. We would like him to discuss his results.*

DR. FOLEY: First of all, I think histamine is in many ways the ideal vasodilator, at least on theoretical grounds. It is a natural substance. It is nature's own vasodilator. Its defects are that its action is fleeting as well as general. In an effort to eliminate the general action the idea has been advanced that one might inject the artery supplying the limb that needed the vasodilatation and thus perfuse the limb with histamine. If the drug is injected slowly into the artery it acts locally in the tissues and little of it reaches the venous side or into the systemic circulation to produce severe headache, a common reaction to histamine. The treatment consists in attaching a flask of saline to a needle in an artery to which histamine has been added. The advantage is that local vasodilatation results. In such extremely sensitive structures as arteries, if they are irritated or traumatized even to the slightest degree, spasm of the artery

itself is apt to be severe, and this is a real disadvantage. In experimental animals we have sometimes stuck needles into the femoral artery and produced such spasm that we could not pull the needle out again.

The second disadvantage is trauma to the artery. If the vessel is arteriosclerotic, a plaque may be rubbed off and embolus occur. We used this treatment in the clinic some years ago. This was before we came to the realization that blood flow and vasodilatation would be so greatly influenced by exercise. If the patient gets up and walks, a greater increase in blood flow would result than from an injection of histamine which would take two hours to administer.

MODERATOR WRIGHT: In other words, we are somewhat iconoclastic about the use of generalized vasodilators. When the entire blood vascular bed is dilated, or a very large portion of it, at one time, unless the blood volume is increased, it is hard to conceive how the blood flow to a leg or a foot that is painful and where the vessels are in spasm can be increased. Under such circumstances that extremity is that portion of the body that is most resistant to easy vasodilatation. Therefore the vessels of the rest of the body dilate more freely than in the involved area. This suggests that perhaps one actually decreases the blood flow in an affected limb.

DR. FOLEY: Could I put in a plug at this time for nitroglycerin? If one wants to release spasm of large vessels or medium sized vessels such as the radial, ulnar, femoral, or popliteal arteries, nitroglycerin has the most profound effect, is easiest to administer and has fewer side effects and dangers than any of the other vasodilators.

MODERATOR WRIGHT: *Is it not true, however, that this dilatation is confined to arteries and does not affect arterioles and capillaries?*

DR. FOLEY: Yes, sir. If one finds a fairly good pulse volume in the radial or ulnar, one won't get any increase in the warmth of the hand but if the patient is having a spasm at the moment, such as Raynaud's spasm and the fingers are white, one can get immediate release of this spasm with nitroglycerin and increased warmth of the fingers.

MODERATOR WRIGHT: *We shall now discuss the question of anticoagulants. We shall not attempt a general discussion of anticoagulants because time does not permit. Dr. Foley, in the treatment of acute arterial occlusion, do you use anticoagulants or not and, if so, what do you use?*

DR. FOLEY: For acute occlusion, we use heparin for its immediate

effect, for the following reasons: First, to limit the propagation of the clot; second, to prevent thrombosis in situ, in the stagnant flow of blood in the capillary bed and veins; third, to prevent further embolization.

MODERATOR WRIGHT: *Dr. Mendlowitz, do you use anticoagulants?*

DR. MENDLOWITZ: We do. We use heparin for its effect in the acute stage and then we follow that by some member of the coumarin group.

MODERATOR WRIGHT: *Dr. Lord, do you have any further comments on this? Do you agree?*

DR. LORD: I agree.

MODERATOR WRIGHT: That is a fair summary of the reaction of this panel. A question which is frequently asked concerns the choice of anticoagulants. It is clear that most of us use heparin for the immediate effect. I think most of the members of this panel would agree that it does not make too much difference which of the coumarins or indanediones you use, providing you know how to use them. In other words, one may use Dicumarol, Hedulin, Tromexan or Marcumar or any of the others. Each has slight advantages or disadvantages according to what one tries to accomplish. If a physician knows how to use any one of these drugs he can obtain essentially the same desired effect.

The panel has permitted me to review a list of what we no longer consider to be essential therapy. If any one of the panel wishes to make a statement in reference to any of these modalities there will be opportunity to do so. We consider that the Pavex boot and the intermittent venous occlusion machine are now discarded therapy; that alpha-tocopherol, or vitamin E, is no longer used. The same may be stated regarding intravenous ether, histidine and ascorbic acid. The use of refrigeration to save a leg is unsound but refrigeration to prepare a leg for amputation is justified in some cases where a severe infection is present in an old diabetic. It may be used for a day or two, prior to amputation. The direct use of heat, of diathermy or heat pads should be discouraged.

Are there any comments regarding these statements? If there are none, we have time for a few questions. Here is the first question: Dr. Lazzarini, why do arterial homografts "take" whereas homografts of most other tissues do not?

DR. LAZZARINI: The idea of the vascular homograft surviving in the host is not correct in a biological sense. There is no demonstrable

viable homograft on any occasion. It has been shown to be nothing more than framework for the host cells to grow in, a sort of mechanical frame and it always will be replaced in a given time by the host vessel.

MODERATOR WRIGHT: *Dr. Mendlowitz, will you please discuss the value of Arlidin in occlusive arterial disease?*

DR. MENDLOWITZ: I cannot answer that specifically. I think it is of some value but no more so than other vasodilators in common use.

MODERATOR WRIGHT: *Dr. Foley!*

DR. FOLEY: I agree with that statement but I think it is a bit hedged. I would like to counter by asking, how often do you prescribe it?

DR. MENDLOWITZ: Very rarely.

MODERATOR WRIGHT: Today we have a choice of about 20 so-called vasodilators. For most of them, the evidence regarding their value in the treatment of arterial occlusion is very slim.

DR. LORD: In all honesty, Dr. Wright, there is no sense in prescribing any of them except that it makes you, as a doctor, feel you are doing something.

MODERATOR WRIGHT: As a matter of fact, that was the implication of my comment of a few minutes ago when I suggested that the affected limb was often the one which received the least increase in blood flow from any general vasodilator.

Dr. Foley, how do you use heparin and how do you control the dosage?

DR. FOLEY: For its immediate effect I use the heparin intravenously but only for the first dose. Since concentrated heparin is now easily obtainable, I use this subcutaneously. The average dose is 15,000 units for a 150 pound man and may be repeated every 12 hours. The coagulation time has to be controlled. A test is done before heparin is given. By the bedside technique that I use, the normal time is 4 to 6 minutes. Five hours after an appropriate subcutaneous dose of heparin the coagulation time should be tripled. I have also used this concentrated heparin for long-term administration in patients who did not respond to other types of anticoagulants. One patient has been kept on it for three months. He administers it to himself every 12 hours, just like a patient taking insulin.

MODERATOR WRIGHT: *Dr. Mendlowitz, do you advise the use of histamine iontophoresis locally over intact but affected skin?*

DR. MENDLOWITZ: No, sir.

MODERATOR WRIGHT: *Does any panel member?*

DR. LORD: No.

MODERATOR WRIGHT: *I will try to answer the next question: Are sympathectomized patients more sensitive to tobacco than before surgery?* My belief is that they are no more so but that they are just as sensitive as before operation. They certainly are no less sensitive.

Another question asks what is the status of the use of fibrinolysin, plasmin or streptokinase in the disintegration of clots and do they hold any promise for the future?

I think the use of all of these preparations is highly experimental at present. They are very interesting compounds, especially plasmin. We are doing some work with it. It is an extremely interesting substance but the lots that have been prepared commercially have not been well standardized and they have produced undesirable reactions. In using these very active substances, the question arises as to whether they present the risk of causing the breaking off and liberation into the circulation of loose emboli from the long slender tail of a thrombus. It is quite possible that these substances may prove useful but further experimental investigation is necessary before they are used in general practice.

Is there any difference of opinion in this regard? If not, Dr. Foley, how do you treat an ulcer of diabetic neuritis located on the sole of the foot?

DR. FOLEY: That is a real tough one, on the sole of the foot. First of all we have a podiatrist provide pads to shift the weight-bearing surface over to another area that is better able to stand it. Since these patients' tissues tend to atrophy when they are confined to bed, we keep them walking. We have used all the other modalities that have been mentioned today.

MODERATOR WRIGHT: *Dr. Lord, in the operation of lumbar sympathectomy, do you favor removal of the 1st, 2nd, 3rd and 4th lumbar ganglia?*

DR. LORD: That is a highly esoteric problem. This is an awful confession. We really don't know what we are doing. We take out all the ganglia we can get from the diaphragm down to where the iliac artery crosses over. Although it was strongly advised years ago to perform a preganglionic sympathectomy and not a postganglionic sympathectomy, this differentiation has largely been discarded at the present time. One does everything possible to remove the sympathetic nerves. Actually, sympathectomy under such conditions seems to be permanent in the

lower extremity. I don't think that is a problem.

MODERATOR WRIGHT: *Dr. Lord, some patients ask the following question before and some ask it after surgery: Does this type of sympathectomy affect the potency of the male?*

DR. LORD: If the operation is done bilaterally, the individual has everything he had before except the ability to ejaculate. It is the opinion of my chief, Dr. William Hinton, that most of the people who require this type of operation don't have to be concerned about that.

MODERATOR WRIGHT: Some of them do, though.

I shall try to answer the next question: How do you treat nocturnal calf pain?

We elevate the head of the bed six or eight inches. We use reflex heat, by putting a heating pad over the abdomen and encourage the person to use the muscles. There are several other things to do for night cramps. One is the use of quinine which frequently stops them although we really do not know why. I have been able to relieve a number of people of night cramps by teaching them the simple technique of stretching their legs with the heels extended instead of the toes extended. For some reason most people tend to stretch their legs with the toes extended and this may cause a tonic contraction of the calf muscles with accompanying cramp pain. It is also important to have the bed clothes loose at the foot of the bed. Many people suffer from cramps because they are too neat, they tuck the bed clothes in tightly thus binding the feet down and fatiguing the muscles by constant prolonged pressure. This is a common cause of cramps,—the treatment is simple and obvious.

One doctor's wife went to eight or ten doctors, including an orthopedist, and bought expensive shoes without any improvement. My only advice to her was to kick the bed clothes free. Her husband called up about two weeks later and said, "Life is heaven again. We have not slept this well in years." About four years later he came up to me at a medical meeting and said, "I want to tell you that you just changed our whole life." A strange way to acquire a patient's appreciation!

This concludes our panel meeting. Thank you all very much!

HYPERVAGISM AND CARDIAC ARREST*

CHARLES H. BAUER, MARY ALLEN ENGLE AND ROBERT MELLINS

INTRODUCTION

REPEATED episodes of cardiac arrest due to sino-auricular block secondary to vagal stimulation are unusual. In 1957 Davies[1] reported two adults with sino-auricular block due to intrathoracic growths stimulating the vagus nerve. These patients had recurrent attacks of syncope, preceded by sinus bradycardia and prevented by atropine. Necropsy demonstrated intrathoracic tumors encircling the vagus nerve. It is the purpose of this paper to report two infants with this arrhythmia and masses closely associated with the vagus nerve.

Case 1:

An eight week old white boy was referred to the New York Hospital because of three episodes of severe cyanosis following crying spells. He was considered healthy until five weeks of age, when the mother noted the presence of lumps on both sides of his neck and in both axillae. These increased progressively in size.

At age seven weeks, following a feeding, the baby suddenly started to cry, turned blue, then black. According to the mother, the baby stopped breathing for the next few minutes. Mouth-to-mouth respiration was given and he was rushed to a hospital. There, within the next week, two similar episodes of cyanosis associated with crying occurred. A physician present during these episodes was unable to obtain a heartbeat. Each time, the child received oxygen by positive pressure and quickly recovered.

Physical examination following transfer to the New York Hospital revealed a small infant whose weight was 3280 gm., only 400 gm. above his birth weight; his height was 50 cm. There was no cyanosis. The chest was clear, and the heart appeared to be normal. The heart rate

* Presented at the meeting of the Section on Pediatrics, January 9, 1958. Manuscript received December 1958.

From the Department of Pediatrics, The New York Hospital-Cornell Medical Center.

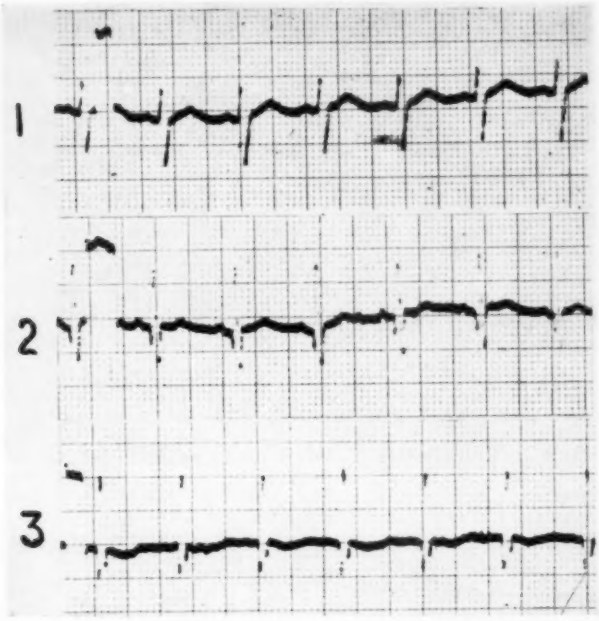

Figure 1. Electrocardiogram taken upon recovery from first observed attack, revealing a regular sinus rhythm.

was 140; marked sinus arrhythmia was present. The other remarkable features of physical examination included a large tongue, a weak, coarse cry, an umbilical hernia, mottled skin, and facial characteristics resembling a cretin. Large, fluid-filled, cystic masses were present on both sides of the neck above the clavicles and in both axillae. These increased in size with crying.

Shortly after admission, the child started to cry, became cyanotic and stopped breathing. Stethoscopic examination revealed *no* heart beat. The baby was unconscious and had a generalized tonic-clonic convulsion. Oxygen, artificial respiration, and peripheral stimulation were employed and the child's color improved; respirations and pulse rate slowly returned to normal. Electrocardiogram taken upon recovery revealed a regular sinus rhythm (Figure 1).

A few minutes later another attack occurred. This time continuous electrocardiograms were recorded while a physician listened to the

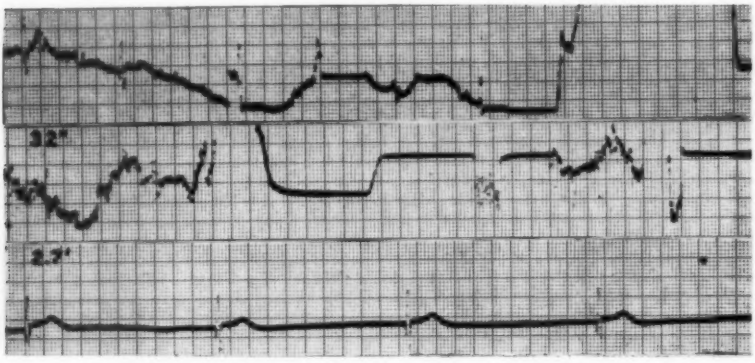

Figure 2. Continuous ECG during a typical attack. Figures in left hand corner indicate time after onset of attack. Top tracing shows slowing and then complete disappearance of heart beats. Also, tracing moves all over paper as patient has a generalized tonic-clonic convulsion (first and second line). 2.7 minutes after onset of attack, baseline is steady as patient has lapsed into coma and A-V nodal rhythm appears.

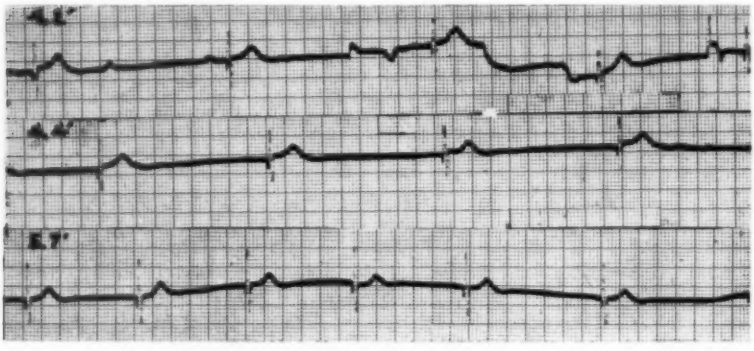

Figure 3. 4.2 minutes:—A sinus beat interrupts the A-V nodal rhythm.
4.4 minutes:—Slow A-V nodal rhythm.
5.7 minutes:—Increase in rate of A-V nodal rhythm.

patient's chest. He developed a generalized tonic-clonic convulsion which caused the electrocardiograph stylus to wander all over the paper (Figure 2). For 2.7 minutes no heart beat was audible or recorded by electrocardiogram. The patient lapsed into coma. Electrocardiogram then showed the appearance of a few heart beats originating in the atrioventricular node at a slow rate (Figure 2). Over the next few

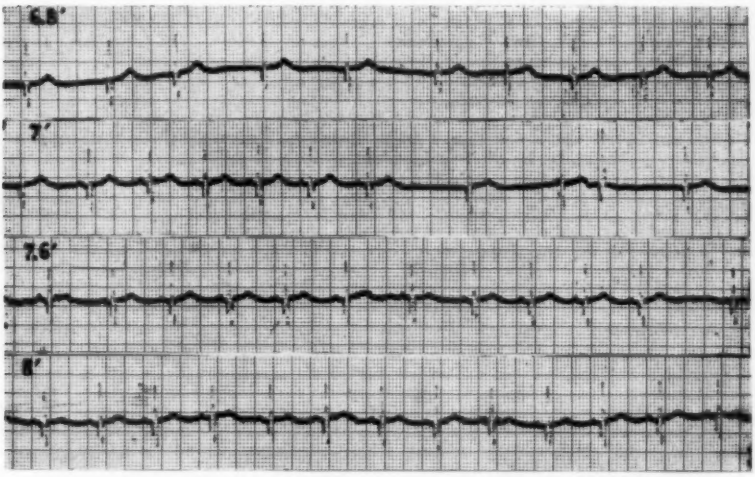

Figure 4. 6.8 minutes:—Further increase in rate of A-V nodal rhythm.
7 minutes:—Sinus rhythm alternating with A-V nodal rhythm.
7.6 minutes:—Sinus rhythm predominates, with only occasional A-V nodal rhythm present.
8 minutes:—Regular sinus rhythm.

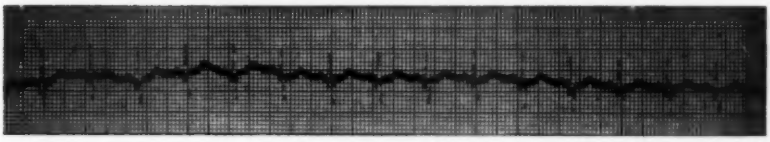

Figure 5. After atropinization, regular sinus rhythm persists even with crying.

minutes the rate increased. The rhythm remained predominantly A-V nodal with only an occasional sinus beat (Figure 3). Seven minutes after the onset of the attack the patient demonstrated predominant sinus rhythm with occasional periods of A-V nodal beats. It was not until eight minutes after the onset of the attack that a regular sinus rhythm at a rate of 140/min. was present (Figure 4). At this time he regained consciousness.

The electrocardiogram was interpreted as showing evidence of sino-atrial block possibly due to hypervagism. Therefore it was decided to treat the next attack with atropine intravenously. An infusion was

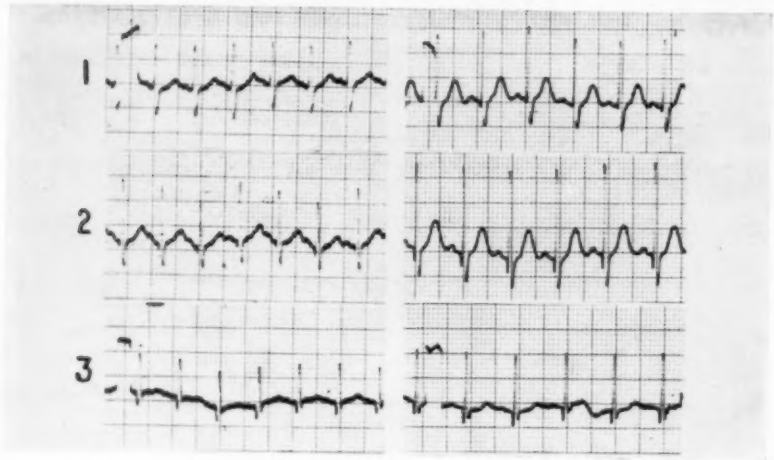

Figure 6. Normal ECG, 3 months (left) and 19 months (right), after onset of attacks while on thyroid medication.

started and when cardiac standstill occurred during a third attack, atropine in a dose of 0.08 mg. was given. Again a slow A-V nodal rhythm appeared, but this time a regular sinus rhythm appeared within two minutes and the attack terminated. There were no further recurrences even with crying (Figure 5). The patient was then atropinized orally (0.1-0.25 mg. every four hours).

The clinical impression of cretinism was confirmed by appropriate laboratory tests, including a PBI of 1.6 micrograms per cent. Thyroid medication in dosage up to 75 mg/day was instituted, and 11 days later the cystic masses in the neck and axillae had disappeared. Atropine was thereupon discontinued without recurrence of cyanosis or bradycardia. Subsequent ECGs, taken three and nine months later, were normal (Figure 6). The patient has grown and is developing normally with maintenance thyroid medication of 120 mg/day. When last seen at the age of 21 months, he was doing well.

Case 2:

The second patient exhibited episodes of bradycardia with sino-atrial block and cyanosis similar to those described in the first child.

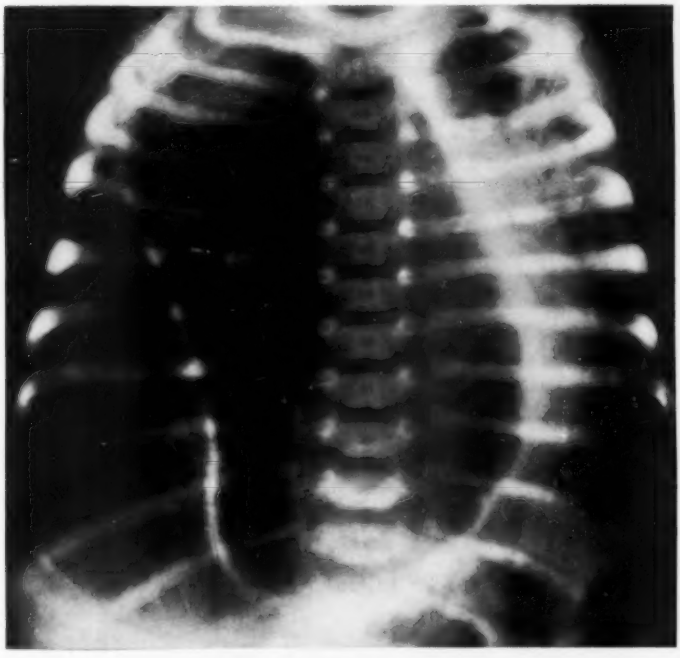

Figure 7. X-ray showing the marked dilatation of the thoracic stomach with displacement of the mediastinal contents to the left.

This infant had an esophagogastrostomy for repair of an esophageal atresia. The stomach was brought into the chest (Figure 7) and, as we later learned, the vagus nerve was compressed by the dilated stomach.

Feedings by polyvinyl tube introduced into the duodenum were well tolerated for the first postoperative month. Nipple feedings, however, resulted in periods of apnea. The electrocardiograms during the attacks showed sino-atrial block and the appearance of slow A-V nodal rhythm as in the first patient. These attacks were relieved by gastric aspiration. Atropine was not used until the last three days of life and then only in small dosage (0.1-0.2 mg. every 12 hours). The patient expired on the 34th postoperative day during one of these episodes of apnea, cyanosis, and bradycardia, before contemplated reconstructive surgery could be performed.

Figure 8. Photograph of necropsy findings. Note the vagus nerve compressed by the dilated stomach.

Photograph of necropsy findings (Figure 8) shows the stomach and first duodenal segment in the right pleural cavity with an esophagogastrostomy at level of T-1 and T-2. The gastric cavity was filled with air and was greatly distended. A valve-like fold occluded the gastroesophageal anastomotic line. The right vagus nerve passed behind the right hilum and was compressed by the dilated stomach.

Discussion

Hypervagism in these babies was manifested by a disturbance in cardiac rhythm due to the depressant action of the vagus nerve on the sinus pacemaker[2]. In the first patient the attacks were probably due to the compression of the carotid sinus by the masses in the neck, especially when the baby cried. Stimulation of the carotid sinus sets up a reflex arc, mediated by the vagus and glossopharyngeal nerves, that results in cardiac standstill followed by syncope and convulsions due to cerebral hypoxia. Atropine protected the patient by abolishing the cardiac effects until the cervical masses disappeared on thyroid therapy[3]. There was no recurrence of the attacks.

We know of a similar infant thought to have classical cystic hygroma. At surgery he was found to have, instead, edema of the tissue. Subsequent laboratory tests showed that these were secondary to hypothyroidism[4]. In our first patient the masses in the neck, localized areas of myxedema, were so strategically located as to give rise to attacks which, in adults, are called "carotid sinus syncope". Weiss[5] has described three types of this syndrome: 1) the "vagal type"—in which syncope results from cerebral hypoxia due to reflex cardiac asystole; 2) the "depressor type"—in which syncope results from cerebral hypoxia due to fall in systemic blood pressure alone; 3) the "cerebral type"—in which syncope ensues without significant change in cardiac rate or blood pressure. The first is by far the most common and explains the events in our patient.

In the second patient, there was intrathoracic stimulation of the vagus nerve by the dilatation of the thoracic stomach, which became further distended during feedings after removal of the duodenal tube. Possibly a more vigorous attempt at atropinization could have prevented the attacks and permitted additional corrective surgery.

Vagus stimulation may have a dual effect on the heart. There may be atrial standstill or slowing, as in these babies, or there may be cardiac acceleration due to the action of the cardiac accelerator fibers arising in the medulla. If atrial standstill occurs, the patient may die in cardiac arrest, as did the second infant, or a slower pacemaker may take over, as the AV node did in the first case.

Atropine was selected as therapy for the attack because, in large doses, it blocks the vagal depressant effects on the sinus pacemaker[6]

and thus leads to resumption of normal sinus rhythm.

The return to a normal rate following administration of atropine in the first case is consistent with sino-atrial block of vagal origin[7].

Bradycardia produced by vagal stimulation could also be treated by epinephrine and other sympathomimetic drugs, like isoproterenol (Isoprel), which act as direct sino-atrial node stimulants. As the primary effect of these drugs is directly on the myocardium, it seemed more physiologic to use atropine, which directly blocks the effects of excessive vagal stimulation.

Summary and Conclusions

Two patients manifesting signs of sino-atrial block due to hypervagism are presented. In one, the basic pathology presumably consisted of localized areas of myxedema and in the other, of a dilated, thoracic stomach. It is important to recognize this form of cardiac arrest since it can be treated effectively. The use of atropine for treatment of the immediate attack and prevention of future episodes is recommended. Correction of the underlying pathology, where possible, is essential for permanent cure.

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UNUSUAL PSYCHIATRIC MANIFESTATIONS OF NEUROLOGICAL DISEASE*

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IN the busy general hospitals throughout the country, more and more psychiatric pavilions, wings or floors are being opened. For many years it has been standard practice in all of the Navy hospitals, to have a neuropsychiatric service, however small, which includes at least one medical officer. (The larger hospitals have several medical officers in the department, headed by a Board-certified psychiatrist.) This medical officer is expected to be moderately competent in both neurology and general clinical psychiatry, which often meets with some critical comment, especially from the younger medical officers, who are primarily trained in psychiatry, with little or no interest in neurology. Also, there is a tendency on the part of the younger men either to fill a disturbed patient with an ataractic drug, or to attempt to admit him directly to a closed psychiatric ward, without an adequate neurological survey as part of the general physical examination.

I would like to cite three cases which were seen on the neuropsychiatric service at St. Albans Naval Hospital, New York, which demonstrate the need for close clinical observation, no matter how "disturbed" the patient may be.

Case No. 1—This patient was a 21 year old Negro male who was admitted for psychiatric and neurological observation because one evening, while sitting at a table eating, at his duty station, he suddenly grasped his head, exclaimed, "Oh, my God" and then became unconscious for a moment. On awakening he seemed confused and disoriented. He began moving his arms and hands rather stiffly in an aimless manner for about one-half hour. He was then able to give a history of flank pain for a week, and of being awakened the night before by a dull headache, then nausea and some relief following a vomiting spell. After admission to the closed ward the patient continued to appear disoriented and confused, the physical examination being otherwise not remarkable. The next

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The opinions expressed herein are those of the writer and are not necessarily to be construed as those of the Navy Department.

morning there was definite stiffness of the neck, nystagmus on lateral gaze to either side and positive Kernig's and Brudzinski's signs. No lateralizing neurological signs were found. A spinal tap revealed a grossly bloody fluid with an initial pressure of 220 mm. of water. The patient was transferred to the neurosurgical service, but was followed by the neuropsychiatric staff. Three days later a second spinal tap revealed an initial pressure of 360 mm. with a grossly bloody fluid. Other examinations were negative, including a skull x-ray. After this the patient improved and a left common carotid arteriogram revealed non-filling of the left anterior cerebral artery. The procedure was well tolerated. The clinical diagnostic impression was that the patient had an acute subarachnoid hemorrhage due to ruptured cerebral aneurysm with subsequent thrombosis of the left anterior cerebral artery. The patient showed a gradual improvement for the next 20 days and then again became unresponsive and made aimless movements of the extremities, similar to those described in the first episode, an aphasia and an adversive turning of the head and eyes to the right. Since it was felt then that the patient had a massive cerebral infarction, surgical intervention was not attempted. He gradually went downhill and expired four days later. Postmortem examination confirmed the diagnosis.

Case No. 2—This patient was a 61 year old white male, retired chief petty officer, who was admitted to the hospital with a history of three days of confusion, disorientation, confabulation and frequent falls. A week previously he had been found on the floor by his neighbor, not unconscious but bleeding from a cut on his nose. He stated that he had fallen over his dog. His son gave a history of the father's having been retired from the Navy 15 years previously because of a coronary thrombosis, and of moderately heavy drinking in recent months, since the patient had been widowed and was living alone, near the son's home. The patient was reported to have varying periods of lucidity in his confusion. Neurological examination revealed only moderately contracted pupils, varying stiffness of the neck, slightly more active deep tendon reflexes on the left and no Babinski. The possibility of the presence of subdural hematoma or a basilar artery occlusion was considered. Immediate electrolyte studies of the blood revealed a sodium of 124 mEq./L as the only abnormality. A lumbar puncture was done without difficulty, the patient tolerating the procedure well. A clear fluid was obtained, with normal dynamics and chemistry. The patient was then considered to be in a low-sodium delirium and was treated with intravenous sodium chloride with potassium chloride added. Within 15 hours the patient's mental status improved and he shortly thereafter was clear and oriented, with some awareness of having been ill. The patient was then moved to an open medical ward where further medical studies were carried out. Though he was transiently confused periodically during the next two weeks, he continued to improve and with proper physiological treatment was able to tolerate well a series of investigations, including a liver biopsy and hepatic catheterization. When liver function returned to normal he was discharged to his home.

Case No. 3—This patient was a 23 year old single white male, midshipman in the Brazilian Navy, who was transferred to the hospital from his ship in the Navy Yard with a diagnosis of "anxiety reaction, acute." There was a history of a recent mild upper respiratory infection with a slight temperature elevation for one day, followed by a complete and sudden change in personality from a conscientious, pleasant and cooperative youth to a negativistic, confused and lethargic patient. On admission to the closed ward, history was unobtainable from the patient due to his negativism and the obvious language barrier. He was noted to be lethargic and posturing. There was no evidence of nuchal rigidity and neurological examination was non-contributory. For two days the patient's condition remained unchanged, except for an increasing dehydration. He remained for long periods in a catatonic-like stupor, assuming bizarre postures. On the third day following admission, the ward nurse, while forcing fluids on the patient, noted a transient strabismus. The patient indicated he had a headache. Physical examination at this time revealed a definite nuchal rigidity and a spinal puncture was done. The pressure was markedly increased, over 300 mm. The cell count revealed 2790 white blood cells with 90 per cent polymorphonuclears, 480 red blood cells, globulin was 3 plus, sugar was 7 mgm per cent, chlorides 645 mgm per cent and protein 117 mgm per cent. Smear of the spinal fluid concentrate revealed many gram-negative extracellular diplococci. A diagnosis of meningococcic meningitis was made and the patient treated with aqueous penicillin and intravenous sulfadiazine. He responded rapidly and within two days was alert and talkative. Within six days he was asymptomatic except for a complaint of diplopia. Examination revealed a paresis of the right lateral rectus muscle. The patient was able to utilize his moderate knowledge of English and to communicate adequately with the hospital personnel. This had been obscured in the early acute phase of his illness. A repeat spinal puncture five weeks after onset of the illness was normal. (No other case of meningitis appeared among the crew of this ship.)

These examples are given to emphasize several points:

1. The line between organic and functional disease is frequently very fine, and there should be only positive reasons for diagnosing either or both in the same patient, one not excluding the other.

2. Any systemic disorder, disturbing the metabolic processes, or any disease activity, may be manifested by a mental disturbance and may also possibly be associated with evidence of nervous system malfunction. One aspect of the total condition cannot be treated successfully while ignoring the other.

3. These phenomena do not obviate or exclude the concurrent psychological processes which are the basis of personality organization and behavior, and which influence the total manifestations of the illness.

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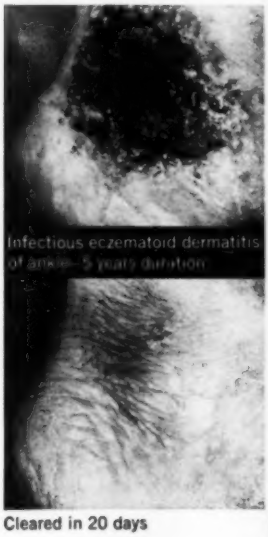

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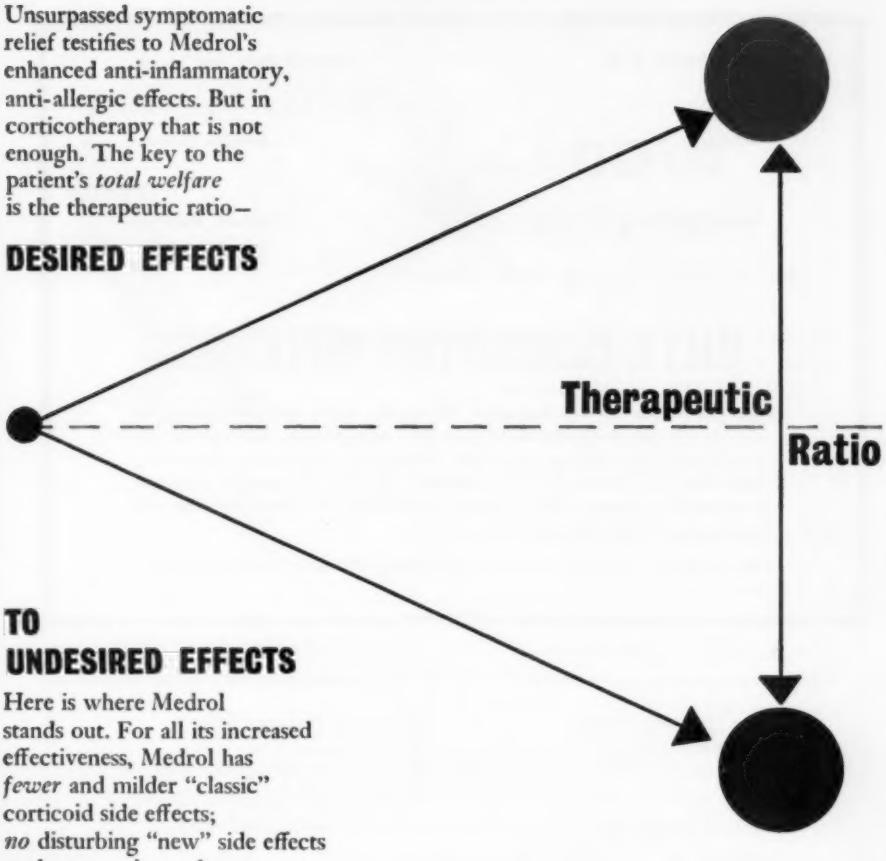

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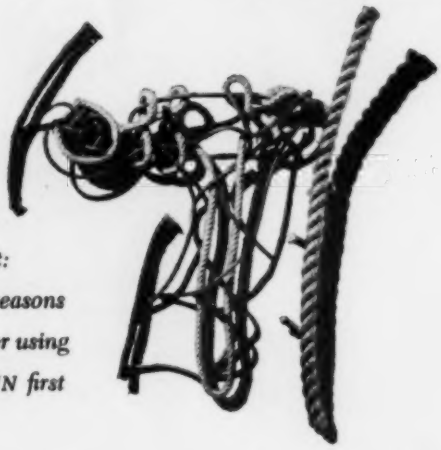

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Available as Tablets, 50 and 100 mg.; Oral Suspension, 25 mg. per 5 cc. tsp.

References: 1. Smith, I. M., and Lenyo, L.: Am. Practitioner 9:78, 1958. 2. Jawetz, E., et al.: A.M.A. Arch. Int. M. 100:549, 1957.

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(1) Vellenga, R. O., and Hood, M. E.: J.A.M.A. 169:652 (June 28) 1957. (2) Bateman, N. J.: Current M. Dig. 25:65 (Jan.) 1958. (3) Koszewski, B. J., and Woods, A. E.: Ann. J. M. Sc. 236:623 (Dec.) 1958. (4) McCarthy, P. E., Hollo, C. E., and Swendseid, M. E.: New England J. Med. 257:1147 (Dec. 12) 1957.

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